AS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION ON SEPTEMBER 15, 2000
REGISTRATION NO. 333-

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM S-1

REGISTRATION STATEMENT

UNDER

THE SECURITIES ACT OF 1933

RIGEL PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

<TABLE>
<S> <C> <C>
DELAWARE 8731 94-3248524
(State or other jurisdiction of incorporation ororganization) (Primary Standard Industrial Classification Code Number) (I.R.S. Employer Identification No.)
</TABLE>

240 EAST GRAND AVENUE
SOUTH SAN FRANCISCO, CALIFORNIA 94080
(650) 624-1100
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

JAMES M. GOWER
PRESIDENT AND CHIEF EXECUTIVE OFFICER
RIGEL PHARMACEUTICALS, INC.
240 EAST GRAND AVENUE
SOUTH SAN FRANCISCO, CALIFORNIA 94080
(650) 624-1100
(Name, address, including zip code, and telephone number, including area code, of agent for service)

COPIES TO:

<TABLE>
<S> <C>
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FIVE PALO ALTO SQUARE
3000 EL CAMINO REAL
PALO ALTO, CA 94306-2155
(650) 843-5000

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525 UNIVERSITY AVENUE, SUITE 220
PALO ALTO, CA 94301
(650) 470-4500
</TABLE>

APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC:
AS SOON AS PRACTICABLE AFTER THE REGISTRATION STATEMENT BECOMES EFFECTIVE.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"), check the following box. / /

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. / /

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. / /

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act

registration number of the earlier effective registration statement for the same offering. / /

If delivery of the Prospectus is expected to be made pursuant to Rule 434, please check the following box. / /

CALCULATION OF REGISTRATION FEE

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TITLE OF SECURITIES TO BE REGISTERED	AMOUNT TO BE REGISTERED(1)	PROPOSED MAXIMUM OFFERING PRICE PER UNIT(2)	PROPOSED MAXIMUM OFFERING PRICE(1)(2)	AMOUNT OF REGISTRATION FEE
<S>	<C>	<C>	<C>	<C>
Common Stock, par value $.001.....	10,350,000	$10.00	$103,500,000	$27,324.00

</TABLE>

(1) Includes 1,350,000 shares of Common Stock issuable upon exercise of the Underwriter's over-allotment option.

(2) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457 under the Securities Act of 1933, as amended.

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT THAT SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(A) OF THE SECURITIES ACT OF 1933 OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(A), MAY DETERMINE.

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PROSPECTUS (SUBJECT TO COMPLETION)

THE INFORMATION IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. WE MAY NOT SELL THESE SECURITIES UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PROSPECTUS IS NOT AN OFFER TO SELL THESE SECURITIES AND IT IS NOT SOLICITING AN OFFER TO BUY THESE SECURITIES IN ANY STATE WHERE THE OFFER OR SALE IS NOT PERMITTED.

ISSUED SEPTEMBER 15, 2000

9,000,000 SHARES

[LOGO]

COMMON STOCK

RIGEL PHARMACEUTICALS, INC. IS OFFERING SHARES OF ITS COMMON STOCK. THIS IS OUR INITIAL PUBLIC OFFERING, AND NO ESTABLISHED PUBLIC MARKET CURRENTLY EXISTS FOR OUR COMMON STOCK. WE ANTICIPATE THAT THE INITIAL PUBLIC OFFERING PRICE WILL BE BETWEEN $8 AND $10.

WE HAVE APPLIED TO HAVE OUR COMMON STOCK APPROVED FOR QUOTATION ON THE NASDAQ NATIONAL MARKET UNDER THE SYMBOL "RIGL."

INVESTING IN THE COMMON STOCK INVOLVES RISKS. SEE "RISK FACTORS" BEGINNING ON PAGE 5.

PRICE $ A SHARE

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	PRICE TO PUBLIC	UNDERWRITING DISCOUNTS AND COMMISSIONS	PROCEEDS TO RIGEL
<S>	<C>	<C>	<C>
PER SHARE.....	$	$	$
TOTAL.....	$	$	$

</TABLE>

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RIGEL PHARMACEUTICALS, INC. HAS GRANTED THE UNDERWRITERS AN OPTION TO PURCHASE UP TO AN ADDITIONAL 1,350,000 SHARES OF OUR COMMON STOCK TO COVER OVER-ALLOTMENTS.

THE SECURITIES AND EXCHANGE COMMISSION AND STATE SECURITIES REGULATORS HAVE NOT APPROVED OR DISAPPROVED THESE SECURITIES, OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

MORGAN STANLEY & CO. INCORPORATED EXPECTS TO DELIVER THE SHARES TO PURCHASERS ON , 2000.

MORGAN STANLEY DEAN WITTER

LEHMAN BROTHERS

ROBERTSON STEPHENS

, 2000

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ABOUT THIS PROSPECTUS

You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of the common stock. In this prospectus, the "Company," "we," "us" and "our" refer to Rigel Pharmaceuticals, Inc.

UNTIL , 2000 (25 DAYS AFTER THE DATE OF THIS PROSPECTUS), ALL DEALERS SELLING SHARES, WHETHER OR NOT PARTICIPATING IN THIS OFFERING, MAY BE REQUIRED TO DELIVER A PROSPECTUS. THIS IS IN ADDITION TO THE DEALERS' OBLIGATION TO DELIVER A PROSPECTUS WHEN ACTING AS UNDERWRITERS AND WITH RESPECT TO THEIR UNSOLD ALLOTMENTS OR SUBSCRIPTIONS.

"Rigel" and the Rigel logo are trademarks of Rigel Pharmaceuticals, Inc. Other trademarks and trade names appearing in this prospectus are the property of their holders.

Rigel was incorporated in Delaware on June 14, 1996. Our principal executive offices are located at 240 East Grand Avenue, South San Francisco, California 94080. Our telephone number is (650) 624-1100. Our website is http://www.rigel.com. The information found on our website is not intended to be a part of this prospectus.

PROSPECTUS SUMMARY

THIS SUMMARY HIGHLIGHTS INFORMATION CONTAINED ELSEWHERE IN THIS PROSPECTUS. THIS SUMMARY MAY NOT CONTAIN ALL OF THE INFORMATION THAT YOU SHOULD CONSIDER BEFORE DECIDING TO INVEST IN OUR COMMON STOCK. WE URGE YOU TO READ THIS ENTIRE PROSPECTUS CAREFULLY, INCLUDING THE "RISK FACTORS" SECTION AND OUR FINANCIAL STATEMENTS AND THE NOTES TO THESE STATEMENTS.

OUR BUSINESS

We use post-genomics combinatorial biology technology to discover novel drug targets. Post-genomics combinatorial biology technology is designed to identify molecules which play an important role in regulating a human cell's response to disease by testing a very large number of proteins in a very large number of cells to determine which proteins will change the cell's response to the disease. Our technology provides a new and rapid way to find those protein molecules and to confirm or validate the role of those molecules in disease without first knowing the identity or sequence of the genes involved. We can identify those protein molecules that may be drug targets by creating a disease-like setting that enables us to detect a change in the cellular response. By creating a map of these protein molecules and their interactions in cells that are involved in a disease process, we can select for drug development protein targets that are specific to the diseases we study and reduce the probability of developing drugs with significant side effects. After selecting these targets, we continue drug development with the goal of developing small molecule drugs. Small molecule drugs are chemical compounds which provide the advantage that they can generally be administered orally. In our first three and one-half years of research, we have succeeded in identifying 22 new drug targets in eight of our nine programs and have generated compounds in five of our programs, including compounds which are candidates for preclinical testing in two of these programs. Our technology is applicable across a broad range of diseases and disorders. We currently have programs in asthma/allergy, autoimmunity, transplant rejection, rheumatoid arthritis, inflammatory bowel disease and cancerous tumor growth. We have a collaboration with Pfizer Inc. and multi-year collaborations with Cell Genesys, Inc., Janssen Pharmaceutica N.V. and Novartis Pharma AG. In addition, we have collaborated with Neurocrine Biosciences, Inc. in order to obtain rights to a library of small chemical compounds. We believe that our innovative technology and corporate collaborations enable us to create value through the discovery of novel drug targets.

THE PROBLEM

Pharmaceutical companies face enormous pressure to develop new drugs and are actively seeking to develop drugs that act on previously unknown targets within cells. Despite revolutionary advances made in molecular biology and genomics, until recently only approximately 500 out of thousands of possible drug targets have been identified, and there has been no efficient way to identify additional appropriate targets for drug development. Efforts to identify the sequence of the complete set of human genes have generated huge amounts of fundamentally important genetic information, and these efforts have provided useful information about which particular genes are associated with particular disease conditions. However, there has been limited progress using this information to identify drug targets quickly and systematically. The result is a shortage of validated drug targets and limited tools to determine which new targets have clinical promise.

OUR SOLUTION

Our drug target discovery process bypasses the need to know the identity or sequence of the genes. We have developed two core technologies which we believe enhance our ability to simultaneously identify and initially validate new drug targets for further development.

Our retroviral technology introduces up to 100 million different peptides or proteins into an equal number of normal or diseased cells and stimulates the cells to induce a disease-like behavioral response. These cells are then sorted at a rate of up to 60,000 cells per second to collect data on up to five different parameters, which means that a sort of 100 million cells can be completed in approximately half an hour. By analyzing the approximately 500 million resulting data points, we can rapidly identify those few cells containing a protein that interacts with a protein target in a way that causes a cell to change its behavior

from diseased back to normal. We believe we can identify the relatively few targets useful for identifying new drugs and initially validate them in the context of a disease-specific cellular response.

Our pathway mapping technology enables us to map interactions between proteins, identify specific proteins which bind with other proteins and select targets for drug development that are specific to the disease we are seeking to affect, avoiding targets that have a role in other diseases or cells. As a result of mapping the interactions of proteins in cells, we establish comprehensive sets of these interactions, referred to as pathways, which carry

the information or signals necessary to regulate both diseased and normal cells.

We believe that our technologies have a number of advantages over traditional and genomics-based drug discovery approaches, including:

- improved target identification;
- rapid validation of protein targets;
- improved pathway mapping;
- better informed target selection;
- more efficient compound screening; and
- reduced risk of failure in the drug development process.

OUR STRATEGY

Our strategy is to develop a large portfolio of drug candidates, out-license drug candidates at a relatively late stage of development and focus on diseases that represent large unmet medical needs. Also, we plan to focus on developing small molecule drugs delivered to protein targets within cells and to establish strategic collaborations with pharmaceutical and biotechnology companies to enhance product development and commercialization. We structure our collaboration agreements to permit multiple collaborations in each disease area by focusing the scope of our agreements on disease pathways and targets.

PRODUCT DEVELOPMENT PROGRAMS

We currently have six product development programs in immune disorders and three in cancer:

IMMUNE DISORDERS

ASTHMA/ALLERGY. IgE is a class of antibody which plays an important role in the activation of the body's immune system. We have identified compounds that inhibit IgE's role in the secretion of inflammatory factors from mast cells. This program has entered preclinical studies in animal models. In our second program we have identified a novel drug target that regulates the production of IgE in B cells and a compound in this program.

AUTOIMMUNITY AND TRANSPLANT REJECTION. These programs seek selective and specific immune system therapeutics which do not negatively affect the protective activities of the immune system. We have identified novel drug targets in T cells and B cells and have initiated high throughput screening.

RHEUMATOID ARTHRITIS AND INFLAMMATORY BOWEL DISEASE. We are characterizing and developing specific inhibitors of protein-degrading enzymes, named E-3 ubiquitin ligases, and have identified several compounds. We also seek to block the inflammatory signals associated with tumor necrosis factor-alpha pathway, a proven link in the inflammatory process. We have identified and validated several novel members of this signaling pathway.

CANCER

TUMOR GROWTH. We have identified and validated two targets, one of which has entered small molecule compound screening in our program for cell cycle checkpoint control, a process which regulates cell proliferation. We have also identified a preclinical candidate compound which is a potent and non-toxic inhibitor of E-3 ubiquitin ligases. In addition, we have identified drug targets in the pathway associated with angiogenesis, a process of blood vessel formation.

THE OFFERING

Common stock offered by us	9,000,000 shares
Common stock to be outstanding after the offering	39,259,340 shares
Over-allotment option	1,350,000 shares
Use of proceeds	For research and development activities, for financing possible acquisitions and investments in technology, for possibly expanding our facilities as well as for working capital and general corporate purposes.
Dividend policy	We do not intend to pay dividends on our common stock.
Proposed Nasdaq National Market symbol	RIGL

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The 39,259,340 shares of our common stock to be outstanding immediately after the offering is based on 29,148,229 shares outstanding at June 30, 2000. This number:

- includes 24,719,677 shares of common stock issuable upon conversion of all preferred stock outstanding at June 30, 2000;
- includes 1,111,111 shares of common stock to be sold in a private placement to Novartis concurrent with the closing of this initial public offering;
- excludes 5,158,884 shares of our common stock issuable upon the exercise of options outstanding as of June 30, 2000, at a weighted average exercise price of $1.58 per share;
- excludes 540,038 shares of our common stock issuable upon the exercise of warrants as of June 30, 2000, at a weighted average exercise price of $1.16 per share; and
- excludes 2,445,064 additional shares of our common stock available for future grant as of June 30, 2000, of which options to purchase 722,010 shares of common stock were granted through August 31, 2000 under our equity incentive plan; an additional 400,000 shares made available under our employee stock purchase plan; and 300,000 shares of our common stock made available under our non-employee directors' stock option plan.

Except as otherwise indicated, information in this prospectus:

- assumes the automatic conversion of all outstanding shares of our preferred stock into common stock on a one-to-one basis;
- excludes 1,350,000 shares issuable upon the exercise of the underwriters' over-allotment option; and
- assumes the sale of 1,111,111 shares of common stock in a private placement to Novartis concurrent with the closing of this initial public offering at an assumed price of $9.00 per share.

SUMMARY FINANCIAL DATA

The following tables summarize our financial data. The pro forma information contained in the statements of operations data and the balance sheet data gives effect to the automatic conversion of all convertible preferred stock into common stock upon the completion of this offering. The pro forma as adjusted balance sheet data reflects the pro forma balance sheet data at June 30, 2000 adjusted for the sale of 9,000,000 shares of our common stock in this offering at an assumed price to the public of $9.00 per share, after deducting the estimated underwriting discounts, commissions and estimated offering expenses payable by us, and the sale of 1,111,111 shares of common stock in a private placement to Novartis concurrent with the closing of this initial public offering at an assumed price of $9.00 per share.

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	PERIOD FROM INCEPTION (JUNE 14, 1996) THROUGH DECEMBER 31, 1996	YEARS ENDED DECEMBER 31, 1997	1998	1999	SIX MONTHS ENDED JUNE 30, 1999	2000
	(UNAUDITED)				(UNAUDITED)	
	(IN THOUSANDS, EXCEPT PER SHARE AMOUNTS)					
<S>	<C>	<C>	<C>	<C>	<C>	<C>
STATEMENTS OF OPERATIONS DATA:						
Contract revenues from collaborations	$ --	$ --	$ 28	$ 8,984	$ 3,069	$ 6,797
Total operating expenses	133	5,601	10,522	21,064	8,538	17,630
Loss from operations	(133)	(5,601)	(10,494)	(12,080)	(5,469)	(10,833)
Interest income (expense), net	--	85	(110)	(286)	12	32
Net loss	$ (133)	$(5,516)	$(10,604)	$(12,366)	$(5,457)	$(10,801)
Net loss per share, basic and diluted	$ (.12)	$ (2.20)	$ (4.01)	$ (4.39)	$ (2.02)	$ (2.60)
Weighted average shares used in computing net loss per share, basic and diluted	1,089	2,512	2,643	2,818	2,703	4,162
Pro forma net loss per share,						

basic and diluted.....	$ (.52)	$ (.38)
Weighted average shares used in computing pro forma net loss per share, basic and diluted.....	23,996	28,393

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	AS OF JUNE 30, 2000		
BALANCE SHEET DATA	ACTUAL	PRO FORMA	PRO FORMA AS ADJUSTED
		(UNAUDITED) (IN THOUSANDS)	
<S>	<C>	<C>	<C>
Cash and cash equivalents.....	$ 15,694	$ 15,694	$100,024
Working capital.....	8,580	8,580	92,910
Total assets.....	25,516	25,516	109,846
Capital lease obligations, less current portion.....	5,121	5,121	5,121
Deferred stock compensation.....	(5,333)	(5,333)	(5,333)
Accumulated deficit.....	(39,420)	(39,420)	(39,420)
Total stockholders' equity.....	11,258	11,258	95,588

</TABLE>

RISK FACTORS

THE SHARES OF COMMON STOCK THAT WE ARE OFFERING THROUGH THIS PROSPECTUS INVOLVE A SUBSTANTIAL RISK OF LOSS. BEFORE MAKING AN INVESTMENT IN THE COMMON STOCK, YOU SHOULD CAREFULLY READ THIS ENTIRE PROSPECTUS AND SHOULD GIVE PARTICULAR ATTENTION TO THE FOLLOWING RISK FACTORS. THE RISKS THAT WE NOW FORESEE MIGHT AFFECT US TO A GREATER OR DIFFERENT DEGREE THAN WE CURRENTLY EXPECT. THERE ARE A NUMBER OF IMPORTANT FACTORS THAT COULD CAUSE OUR ACTUAL RESULTS TO DIFFER MATERIALLY FROM THOSE INDICATED BY THE FORWARD-LOOKING STATEMENTS CONTAINED IN THIS PROSPECTUS. THESE FACTORS INCLUDE, WITHOUT LIMITATION, THE RISK FACTORS LISTED BELOW AND OTHER FACTORS PRESENTED THROUGHOUT THIS PROSPECTUS.

RISKS RELATED TO OUR BUSINESS

OUR SUCCESS AS A COMPANY IS UNCERTAIN DUE TO OUR LIMITED OPERATING HISTORY, OUR HISTORY OF OPERATING LOSSES AND THE UNCERTAINTY OF FUTURE PROFITABILITY.

Due in large part to the significant research and development expenditures required to identify and validate new drug candidates, we have not been profitable and have generated operating losses since we were incorporated in June 1996. Currently, our revenues are generated solely from research payments from our collaboration agreements and licenses and are insufficient to generate profitable operations. As of June 30, 2000, we had an accumulated deficit of approximately $39.4 million. We expect to incur losses for at least the next several years and expect that these losses will actually increase as we expand our research and development activities, incur significant clinical and testing costs and possibly expand our facilities. Moreover, our losses are expected to continue even if our current research projects are able to successfully identify potential drug targets. If the time required to generate revenues and achieve profitability is longer than anticipated or if we are unable to obtain necessary capital, we may not be able to fund and continue our operations.

BECAUSE MOST OF OUR EXPECTED FUTURE REVENUES ARE CONTINGENT UPON COLLABORATIVE AND LICENSE AGREEMENTS, WE MIGHT NOT MEET OUR STRATEGIC OBJECTIVES.

Our ability to generate revenues in the near term depends on our ability to enter into additional collaborative agreements with third parties and to maintain the agreements we currently have in place. To date, all of our revenue has been related to the research phase of each of our collaborative agreements, which revenue is for specified periods and is partially offset by corresponding research costs. Following the completion of the research phase of each collaborative agreement, additional revenue may come only from milestone payments and royalties, which may not be paid, if at all, until some time well into the future. The risk is heightened due to the fact that unsuccessful research efforts may preclude us from receiving any contingent funding under these agreements. Our receipt of revenue from collaborative arrangements is also significantly affected by the timing of efforts expended by us and our collaborators and the timing of lead compound identification. Under many agreements, milestone payments may not be earned until the collaborator has advanced products into clinical testing, which may never occur or may not occur until some time well into the future.

Our business plan contemplates that we will need to generate meaningful revenues from royalties and licensing agreements. To date, we have not yet received any revenue from royalties for the sale of commercial drugs, and we do

not know when we will receive any such revenue, if at all. Likewise, we have not licensed any lead compounds or drug development candidates to third parties, and we do not know whether any such license will be entered into on acceptable terms in the future, if at all.

We are unable to predict when, or if, we will become profitable and even if we are able to achieve profitability at any point in time, we do not know if our operations will be able to maintain profitability during any future periods.

THERE IS A HIGH RISK THAT EARLY-STAGE DRUG DISCOVERY AND DEVELOPMENT MIGHT NOT SUCCESSFULLY GENERATE GOOD DRUG CANDIDATES.

At the present time, our operations are in the early stages of drug identification and development. To date, we have only identified a few potential drug compounds, all of which are still in very early stages of development and have not yet been put into preclinical or clinical testing. It is statistically unlikely that the few compounds that we have identified as potential drug candidates will actually lead to successful drug development efforts, and we do not expect any drugs resulting from our research to be commercially available for several years, if at all. Our leads for potential drug compounds will be subject to the risks and failures inherent in the development of pharmaceutical products based on new technologies. These risks include, but are not limited to, the inherent difficulty in selecting the right drug target and avoiding unwanted side effects as well as the unanticipated problems relating to product development, testing, regulatory compliance, manufacturing, marketing and competition, and additional costs and expenses that may exceed current estimates.

WE MIGHT NOT BE ABLE TO COMMERCIALIZE OUR DRUG CANDIDATES SUCCESSFULLY IF PROBLEMS ARISE IN THE TESTING AND APPROVAL PROCESS.

Commercialization of our product candidates depends upon successful completion of preclinical studies and clinical trials. Preclinical testing and clinical development are long, expensive and uncertain processes and we do not know whether we, or any of our collaborative partners, will be permitted to undertake clinical trials of any potential products. It may take us or our collaborative partners several years to complete any such testing, and failure can occur at any stage of testing. Interim results of trials do not necessarily predict final results, and acceptable results in early trials may not be repeated in later trials. A number of companies in the pharmaceutical industry, including biotechnology companies, have suffered significant setbacks in advanced clinical trials, even after promising results in earlier trials. Moreover, if and when our projects reach clinical trials, we or our collaborative partners may decide to discontinue development of any or all of these projects at any time for commercial, scientific or other reasons. There is also a risk that competitors and third parties may develop similar or superior products or have proprietary rights that preclude us from ultimately marketing our products, as well as the potential risk that our products may not be accepted by the marketplace.

IF OUR CURRENT CORPORATE COLLABORATIONS OR LICENSE AGREEMENTS ARE UNSUCCESSFUL OR IF CONFLICTS DEVELOP WITH THESE RELATIONSHIPS, OUR RESEARCH AND DEVELOPMENT EFFORTS COULD BE DELAYED.

Our strategy depends upon the formation and sustainability of multiple collaborative arrangements and license agreements with third parties in the future. We rely on these arrangements for not only financial resources, but also for expertise that we expect to need in the future relating to manufacturing, sales and marketing, and for licenses to technology rights. To date, we have entered into five such arrangements with corporate collaborators; however, we do not know if such third parties will dedicate sufficient resources or if any such development or commercialization efforts by third parties will be successful. Should a collaborative partner fail to develop or commercialize a compound or product to which it has rights from us, we may not receive any future milestone payments and will not receive any royalties associated with such compound or product. In addition, the continuation of some of our partnered drug discovery and development programs may be dependent on the periodic renewal of our corporate collaborations. For example, our two-year collaboration with Pfizer is scheduled to expire in January 2001, and we do not expect that this collaboration will be renewed. More generally, our corporate collaboration agreements may terminate before the full term of the collaborations or upon a breach or a change of control. We may not be able to renew these collaborations on acceptable terms, if at all, or negotiate additional corporate collaborations on acceptable terms, if at all.

We are also a party to various license agreements that give us rights to use specified technologies in our research and development processes. The agreements pursuant to which we have in-licensed

technology permit our licensors to terminate the agreements under certain circumstances. If we are not able to continue to license these and future technologies on commercially reasonable terms, our product development and research may be delayed.

Conflicts might also arise with respect to our various relationships with third parties. If any of our corporate collaborators were to breach or terminate their agreement with us or otherwise fail to conduct the collaborative activities successfully and in a timely manner, the preclinical or clinical development or commercialization of the affected product candidates or research programs could be delayed or terminated. We generally do not control the amount and timing of resources that our corporate collaborators devote to our programs or potential products. We do not know whether current or future collaborative partners, if any, might pursue alternative technologies or develop alternative products either on their own or in collaboration with others, including our competitors, as a means for developing treatments for the diseases targeted by collaborative arrangements with us. Conflicts also might arise with collaborative partners concerning proprietary rights to particular compounds. While our existing collaborative agreements typically provide that we retain milestone payments and royalty rights with respect to drugs developed from certain derivative compounds, any such payments or royalty rights may be at reduced rates and disputes may arise over the application of derivative payment provisions to such drugs, and we may not be successful in such disputes.

IF WE FAIL TO ENTER INTO NEW COLLABORATIVE ARRANGEMENTS IN THE FUTURE, OUR BUSINESS AND OPERATIONS WOULD BE NEGATIVELY IMPACTED.

Although we have established several collaborative arrangements and various license agreements, we do not know if we will be able to establish additional arrangements, or whether current or any future collaborative arrangements will ultimately be successful. For example, there have been and may continue to be a significant number of recent business combinations among large pharmaceutical companies that have resulted and may continue to result in a reduced number of potential future corporate collaborators, which may limit our ability to find partners who will work with us in developing and commercializing our drug targets. If business combinations involving our existing corporate collaborators were to occur, the effect could be to diminish, terminate or cause delays in one or more of our corporate collaborations.

WE WILL NEED ADDITIONAL CAPITAL IN THE FUTURE TO SUFFICIENTLY FUND OUR OPERATIONS AND RESEARCH.

We will require additional financing in the future to fund our operations. Our operations require significant additional funding in large part due to our research and development expenses, future preclinical and clinical-testing costs, the possibility of expanding our facilities and the absence of any meaningful revenues over the foreseeable future. The amount of future funds needed will depend largely on the success of our collaborations and our research activities and we do not know whether additional financing will be available when needed, or that, if available, we will obtain financing on terms favorable to our stockholders or us. We have consumed substantial amounts of capital to date and operating expenditures are expected to increase over the next several years as we expand our infrastructure and research and development activities.

We believe that the net proceeds from this offering, together with the proceeds from the concurrent private placement with Novartis, will be sufficient to support our current operating plan through at least the next 24 months. Nonetheless, our future funding requirements will depend on many factors, including, but not limited to:

- any changes in the breadth of our research and development programs;
- the results of research and development, preclinical studies and clinical trials conducted by us or our collaborative partners or licensees, if any;
- the acquisition or licensing of technologies or compounds, if any;

- our ability to maintain and establish new corporate relationships and research collaborations;
- our ability to manage growth;
- competing technological and market developments;
- the time and costs involved in filing, prosecuting, defending and enforcing patent and intellectual property claims;
- the receipt of contingent licensing or milestone fees from our current or future collaborative and license arrangements, if established; and
- the timing of regulatory approvals.

To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. To the extent that we raise additional funds through collaboration and licensing arrangements, we may be required to relinquish some rights to our technologies or product candidates, or grant licenses on terms that are not favorable to us. If adequate funds are not available, we will not be able to continue developing our products.

OUR SUCCESS IS DEPENDENT ON INTELLECTUAL PROPERTY RIGHTS HELD BY US AND THIRD PARTIES AND OUR INTEREST IN SUCH RIGHTS IS COMPLEX AND UNCERTAIN.

Our success will depend to a large part on our own, our licensees' and our licensors' ability to obtain and defend patents for each party's respective technologies and the compounds and other products, if any, resulting from the application of such technologies. One patent has been issued to us as of the date of this prospectus, and we have numerous applications awaiting approval. In the future, our patent position might be highly uncertain and involve complex legal and factual questions. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date. Accordingly, we cannot predict the breadth of claims allowed in our or other companies' patents.

The degree of future protection for our proprietary rights is uncertain and we cannot ensure that:

- we were the first to make the inventions covered by each of our pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not independently develop similar or alternative technologies or duplicate any of our technologies;
- any of our pending patent applications will result in issued patents;
- any patents issued to us or our collaborators will provide a basis for commercially viable products or will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies that are patentable; or
- the patents of others will not have a negative effect on our ability to do business.

We rely on trade secrets to protect technology where we believe patent protection is not appropriate or obtainable. However, trade secrets are difficult to protect. While we require employees, collaborators and consultants to enter into confidentiality agreements, we may not be able to adequately protect our trade secrets or other proprietary information in the event of any unauthorized use or disclosure or the lawful development by others of such information.

We are a party to certain in-license agreements which are important to our business, and we generally do not control the prosecution of in-licensed technology. Accordingly, we are unable to exercise the same degree of control over this intellectual property as we exercise over our internally developed technology. Moreover, some of our academic institution licensors, research collaborators and scientific advisors have

rights to publish data and information in which we have rights. If we cannot maintain the confidentiality of our technology and other confidential information in connection with our collaborations, then our ability to receive patent protection or protect our proprietary information will be impaired. In addition, some of the technology we have licensed relies on patented inventions developed using U.S. government resources. The U.S. government retains certain rights, as defined by law, in such patents, and may choose to exercise such rights.

For additional information concerning our intellectual property, see "Business--Intellectual Property."

IF A DISPUTE ARISES REGARDING THE INFRINGEMENT OR MISAPPROPRIATION OF THE PROPRIETARY RIGHTS OF OTHERS, SUCH DISPUTE COULD BE COSTLY AND RESULT IN DELAYS IN OUR RESEARCH AND DEVELOPMENT ACTIVITIES.

Our success will also depend, in part, on our ability to operate without infringing on or misappropriating the proprietary rights of others. There are many issued patents and patent applications filed by third parties relating to products or processes that are similar or identical to ours or our licensors, and others may be filed in the future. There can be no assurance that our activities, or those of our licensors, will not infringe patents owned by others. We believe that there may be significant litigation in the industry regarding patent and other intellectual property rights, and we do not know if we or our collaborators would be successful in any such litigation. Any legal action against our collaborators or us claiming damages or seeking to enjoin commercial activities relating to the affected products, our methods or processes could:

- require our collaborators or us to obtain a license to continue to use, manufacture or market the affected products, methods or processes, which may not be available on commercially reasonable terms, if at all;

- prevent us from using the subject matter claimed in the patents held by others;

- subject us to potential liability for damages;

- consume a substantial portion of our managerial and financial resources; and

- result in litigation or administrative proceedings which may be costly, whether we win or lose.

M&E Biotech A/S, a Danish biotechnology company, has notified us that it expects to receive patent protection in European countries for a process similar to certain aspects of our technologies. M&E has indicated a willingness to license their intellectual property to us but has not specified the terms for the license. We are currently reviewing their patent file and evaluating whether or not to seek a license. In the event we desire to seek a license from M&E, we may not be able to obtain a license on acceptable terms. Furthermore, such failure might adversely impact our collaborations with European partners or may materially adversely affect our business in the jurisdictions that may be covered by the patent protection. We are also aware that M&E has the option to seek patent protection in other parts of the world, including the U.S., for the technology of its European patent protection. If M&E were to receive such patent protection, it might conflict with or overlap with the patent rights we are pursuing. We currently do not, and do not plan to, operate in any country outside the United States.

We are aware of the existence of a United States patent directed towards a general cloning system. It is possible that this patent could be construed to cover certain aspects of our technologies. If legal action were initiated on this patent, it could have the effects discussed above.

IF WE ARE UNABLE TO OBTAIN REGULATORY APPROVAL TO MARKET PRODUCTS IN THE UNITED STATES AND FOREIGN JURISDICTIONS, WE MIGHT NOT BE PERMITTED TO COMMERCIALIZE PRODUCTS FROM OUR RESEARCH.

Due, in part, to the early stage of our drug candidate research and development process, we cannot predict whether regulatory clearance will be obtained for any product we or our collaborative partners

hope to develop. Satisfaction of regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product and requires the expenditure of substantial resources. Of particular significance to us are the requirements covering research and development and testing.

Before commencing clinical trials in humans, we, or our collaborative partners, will need to submit and receive approval from the FDA of an Investigational New Drug application, or IND. If regulatory clearance of a product is granted, this clearance will be limited to those disease states and conditions for which the product is demonstrated through clinical trials to be safe and efficacious. We cannot ensure that any compound developed by us, alone or with others, will prove to be safe and efficacious in clinical trials and will meet all of the applicable regulatory requirements needed to receive marketing clearance.

Outside the United States, our ability or that of our collaborative partners to market a product is contingent upon receiving a marketing authorization from the appropriate regulatory authorities. This foreign regulatory approval process typically includes all of the risks associated with FDA clearance described above and may also include additional risks.

For additional information concerning the regulatory approval process, see "Business--Government Regulation."

WE MAY ENCOUNTER DIFFICULTIES IN MANAGING OUR GROWTH AND THESE DIFFICULTIES COULD INCREASE OUR LOSSES.

We have experienced a period of rapid and substantial growth that has placed and will continue to place a strain on our human and capital resources. The number of our employees increased from 31 at December 31, 1997 to 102 at August 31, 2000. Our ability to manage our operations and growth effectively requires us to continue to use funds to improve our operational, financial and management controls, reporting systems and procedures and to attract and retain sufficient numbers of talented employees. If we are unable to manage this growth effectively, our losses will increase.

IF OUR COMPETITORS DEVELOP TECHNOLOGIES THAT ARE MORE EFFECTIVE THAN OURS, OUR COMMERCIAL OPPORTUNITY WILL BE REDUCED OR ELIMINATED.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. Many of the drugs that we are attempting to discover will be competing with existing therapies. In addition, a number of companies are pursuing the development of pharmaceuticals

that target the same diseases and conditions that we are targeting. We face competition from pharmaceutical and biotechnology companies both in the United States and abroad. Our competitors may utilize discovery technologies and techniques or partner with collaborators in order to develop products more rapidly or successfully than we or our collaborators are able to do. Many of our competitors, particularly large pharmaceutical companies, have substantially greater financial, technical and human resources than we do. In addition, academic institutions, government agencies and other public and private organizations conducting research may seek patent protection with respect to potentially competitive products or technologies and may establish exclusive collaborative or licensing relationships with our competitors.

We believe that our ability to compete is dependent, in part, upon our ability to create, maintain and license scientifically advanced technology and upon our and our strategic partners' ability to develop and commercialize pharmaceutical products based on this technology, as well as our ability to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary technology or processes and secure sufficient capital resources for the expected substantial time period between technological conception and commercial sales of products based upon our technology. The failure by us or any of our collaborators in any of those areas may prevent the successful commercialization of our potential drug targets.

Our competitors might develop technologies and drugs that are more effective or less costly than any which are being developed by us or which would render our technology and potential drugs obsolete and noncompetitive. In addition, our competitors may succeed in obtaining the approval of the FDA or other regulatory approvals for drug candidates more rapidly than us or our strategic partners. Companies that complete clinical trials, obtain required regulatory agency approvals and commence commercial sale of their drugs before their competitors may achieve a significant competitive advantage, including certain patent and FDA marketing exclusivity rights that would delay or prevent our ability to market certain products. Any drugs resulting from our research and development efforts, or from our joint efforts with our existing or future collaborative partners, might not be able to compete successfully with competitors' existing or future products or products under development or obtain regulatory approval in the United States or elsewhere.

OUR ABILITY TO GENERATE REVENUES WILL BE DIMINISHED IF OUR COLLABORATIVE PARTNERS FAIL TO OBTAIN ACCEPTABLE PRICES OR AN ADEQUATE LEVEL OF REIMBURSEMENT FOR PRODUCTS FROM THIRD-PARTY PAYORS.

The drugs we hope to develop may be rejected by the marketplace due to many factors, including cost. Our ability to commercially exploit a drug may be limited due to the continuing efforts of government and third-party payors to contain or reduce the costs of health care through various means. For example, in some foreign markets, pricing and profitability of prescription pharmaceuticals are subject to government control. In the United States, we expect that there will continue to be a number of federal and state proposals to implement similar government control. In addition, increasing emphasis on managed care in the United States will likely continue to put pressure on the pricing of pharmaceutical products. Cost control initiatives could decrease the price that any of our collaborators would receive for any products in the future. Further, cost control initiatives could adversely affect our collaborators' ability to commercialize our products and our ability to realize royalties from this commercialization.

Our ability to commercialize pharmaceutical products with collaborators may depend in part on the extent to which reimbursement for the products will be available from:

- government and health administration authorities;

- private health insurers; and

- other third-party payors.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Third-party payors, including Medicare, are challenging the prices charged for medical products and services. Government and other third-party payors increasingly are attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for new drugs and by refusing, in some cases, to provide coverage for uses of approved products for disease indications for which the FDA has not granted labeling approval. Third-party insurance coverage may not be available to patients for any products we discover and develop, alone or with collaborators. If government and other third-party payors do not provide adequate coverage and reimbursement levels for our products, the market acceptance of these products may be reduced.

IF CONFLICTS ARISE BETWEEN OUR COLLABORATORS OR ADVISORS AND US, ANY OF THEM MAY ACT IN THEIR SELF-INTEREST, WHICH MAY BE ADVERSE TO YOUR INTERESTS.

If conflicts arise between us and our corporate collaborators or scientific advisors, the other party may act in its self-interest and not in the interest

of our stockholders. Some of our corporate collaborators are conducting multiple product development efforts within each disease area that is the subject of the collaboration with us. In some of our collaborations, we have agreed not to conduct independently, or with any third party, any research that is competitive with the research conducted under our collaborations. Our collaborators, however, may develop, either alone or with others, products in related fields that are

competitive with the products or potential products that are the subject of these collaborations. Competing products, either developed by our collaborators or to which our collaborators have rights, may result in their withdrawal of support for our product candidates.

IF PRODUCT LIABILITY LAWSUITS ARE SUCCESSFULLY BROUGHT AGAINST US, WE MAY INCUR SUBSTANTIAL LIABILITIES AND MAY BE REQUIRED TO LIMIT COMMERCIALIZATION OF OUR PRODUCTS.

The testing and marketing of medical products entail an inherent risk of product liability. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our products. We currently do not have product liability insurance and our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of pharmaceutical products we develop, alone or with corporate collaborators. We or our corporate collaborators might not be able to obtain insurance at a reasonable cost, if at all. While under various circumstances we are entitled to be indemnified against losses by our corporate collaborators, indemnification may not be available or adequate should any claim arise.

OUR RESEARCH AND DEVELOPMENT EFFORTS WILL BE SERIOUSLY JEOPARDIZED IF WE ARE UNABLE TO ATTRACT AND RETAIN KEY EMPLOYEES AND RELATIONSHIPS.

Being a small company with only 102 employees as of August 31, 2000, our success depends on the continued contributions of our principal management and scientific personnel and on our ability to develop and maintain important relationships with leading academic institutions, scientists and companies in the face of intense competition for such personnel. In particular, our research programs depend on our ability to attract and retain highly skilled chemists and other scientists. If we lose the services of any of our personnel, including, in particular, Donald Payan, our research and development efforts could be seriously and adversely affected. Although we generally have not experienced problems retaining key employees, our employees can terminate their employment with us at any time. We also expect to encounter increasing difficulty in attracting enough qualified personnel as our operations expand and the demand for these professionals increases, and this difficulty could impede significantly the achievement of our research and development objectives.

WE DEPEND ON OUR SCIENTIFIC ADVISORS FOR THE SUCCESS AND CONTINUATION OF OUR RESEARCH EFFORTS.

We are dependent on the members of our Scientific Advisory Board (SAB) and Clinical Advisory Board (CAB) who conduct research and provide us with access to technology developed by them. The potential success of our drug discovery programs depends in part on continued collaborations with these advisors. We and various members of our management and research staff rely heavily on members of the SAB and CAB for expertise in screening research. Our scientific advisors are not employees of ours and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. All members of the SAB and CAB have entered into scientific advisory agreements with us. These agreements provide for indefinite terms of service on the SAB and CAB and are generally terminable at any time by written notice by either us or the advisor. Certain members of the SAB and CAB also have entered into separate consulting agreements with us. We do not know if we will be able to maintain such consulting agreements or that such scientific advisors will not enter into consulting arrangements, exclusive or otherwise, with competing pharmaceutical or biotechnology companies, any of which would have a detrimental impact on our research objectives and could have a material adverse effect on our business, financial condition and results of operations.

IF WE USE BIOLOGICAL AND HAZARDOUS MATERIALS IN A MANNER THAT CAUSES INJURY OR VIOLATES LAWS, WE MAY BE LIABLE FOR DAMAGES.

Our research and development activities involve the controlled use of potentially harmful biological materials as well as hazardous materials, chemicals and various radioactive compounds. We cannot completely eliminate the risk of accidental contamination or injury from the use, storage, handling or disposal of these materials. In the event of contamination or injury, we could be held liable for damages that result, and any liability could exceed our resources. We are subject to federal, state and local laws and regulations governing the use, storage, handling and disposal of these materials and specified waste products. The cost of compliance with, or any potential violation of, these laws and regulations could be significant.

OUR FACILITIES ARE LOCATED NEAR KNOWN EARTHQUAKE FAULT ZONES, AND THE OCCURRENCE OF AN EARTHQUAKE OR OTHER CATASTROPHIC DISASTER COULD CAUSE DAMAGE TO OUR FACILITIES AND EQUIPMENT, WHICH COULD REQUIRE US TO CEASE OR CURTAIL OPERATIONS.

Our facilities are located in the San Francisco Bay Area near known earthquake fault zones and are vulnerable to significant damage from earthquakes. We are also vulnerable to damage from other types of disasters, including fires, floods, power loss, communications failures and similar events. If any disaster were to occur, our ability to operate our business at our facilities would be seriously, or potentially completely, impaired and our research could be lost or destroyed. In addition, the unique nature of our research activities and of much of our equipment could make it difficult for us to recover from a disaster. The insurance we maintain may not be adequate to cover or losses resulting from disasters or other business interruptions.

RISKS RELATED TO THIS OFFERING

WE MAY ALLOCATE THE NET PROCEEDS FROM THIS OFFERING IN WAYS THAT YOU AND OTHER STOCKHOLDERS MAY NOT APPROVE.

Management will have significant flexibility in applying the net proceeds of this offering and could use these proceeds for purposes other than those contemplated at the time of the offering.

IF OUR OFFICERS, DIRECTORS AND LARGEST STOCKHOLDERS CHOOSE TO ACT TOGETHER, THEY MAY BE ABLE TO CONTROL OUR MANAGEMENT AND OPERATIONS, ACTING IN THEIR BEST INTERESTS AND NOT NECESSARILY THOSE OF OTHER STOCKHOLDERS.

Following completion of the public offering and the concurrent private placement with Novartis, our directors, executive officers and principal stockholders and their affiliates will beneficially own approximately 27.6% of our common stock, based on their beneficial ownership as of August 31, 2000. Accordingly, they collectively will have the ability to determine the election of all of our directors and to determine the outcome of most corporate actions requiring stockholder approval. They may exercise this ability in a manner that advances their best interests and not necessarily those of other stockholders.

THERE MAY NOT BE AN ACTIVE, LIQUID TRADING MARKET FOR OUR COMMON STOCK.

An active trading market for our common stock may not develop following this offering. You may not be able to sell your stock quickly or at the market price if trading in our stock is not active. The initial public offering price will be determined by negotiations between us and the representatives of the underwriters based upon a number of factors. The initial public offering price may not be indicative of prices that will prevail in the trading market.

OUR STOCK PRICE MAY BE VOLATILE AND YOUR INVESTMENT IN OUR STOCK COULD DECLINE IN VALUE.

Prior to this offering, there has been no public market for our common stock, and an active public market for our common stock may not develop or be sustained after the offering. The initial public offering price will be determined by negotiations between the representatives of the underwriters and us and may not be indicative of future market prices. Among the factors to be considered in determining the initial public offering price of the common stock, in addition to prevailing market conditions, will be:

- estimates of our business potential and earnings prospects;
- an assessment of our management; and
- the consideration of the above factors in relation to market valuations of companies in related businesses.

The market prices for securities of biotechnology companies in general have been highly volatile and may continue to be highly volatile in the future. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- announcements of technological innovations or new commercial products by our competitors or us;
- developments concerning proprietary rights, including patents;
- developments concerning our collaborations;
- publicity regarding actual or potential medical results relating to products under development by our competitors or us;
- regulatory developments in the United States and foreign countries;
- litigation;

- economic and other external factors or other disaster or crisis; or

- period-to-period fluctuations in financial results.

IF OUR STOCKHOLDERS SELL SUBSTANTIAL AMOUNTS OF OUR COMMON STOCK AFTER THE PUBLIC OFFERING, THE MARKET PRICE OF OUR COMMON STOCK MAY FALL.

If our stockholders sell substantial amounts of our common stock, including shares issued upon the exercise of outstanding options and warrants, the market price of our common stock may fall. These sales also might make it more difficult for us to sell equity or equity-related securities in the future at a time and price that we deem appropriate. After completion of the public offering and the concurrent private placement to Novartis, we will have 39,259,340 outstanding shares of common stock, which assumes no exercise of outstanding options or warrants after June 30, 2000 and no exercise of the underwriters' over-allotment option.

We intend to file a registration statement on Form S-8 covering an aggregate of 8,139,174 shares issuable upon exercise of options to purchase common stock and common stock reserved for issuance under our stock plans after the effective date of the registration statement of which this prospectus is a part.

ANTI-TAKEOVER PROVISIONS IN OUR CHARTER DOCUMENTS AND UNDER DELAWARE LAW MAY MAKE AN ACQUISITION OF US, WHICH MAY BE BENEFICIAL TO OUR STOCKHOLDERS, MORE DIFFICULT.

Provisions of our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us, even if doing so would benefit our stockholders. These provisions:

- establish that members of the board of directors may be removed only for cause upon the affirmative vote of stockholders owning at least two-thirds of our capital stock;

- authorize the issuance of "blank check" preferred stock that could be issued by our board of directors to increase the number of outstanding shares and thwart a takeover attempt;

- limit who may call a special meeting of stockholders;

- prohibit stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;

- establish advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings; and

- provide for a board of directors with staggered terms.

In addition, Section 203 of the Delaware General Corporation Law may discourage, delay or prevent a third party from acquiring us.

THE PUBLIC OFFERING AND THE CONCURRENT PRIVATE PLACEMENT WILL CAUSE DILUTION IN NET TANGIBLE BOOK VALUE.

Purchasers in the public offering will experience immediate and substantial dilution in the net tangible book value of the common stock from the initial public offering price. Additional dilution is likely to occur upon exercise of options and warrants granted by us.

FORWARD-LOOKING INFORMATION

You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus. This prospectus is not an offer to sell or a solicitation of an offer to buy our common stock in any jurisdiction where it is unlawful. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of common stock. This preliminary prospectus is subject to completion prior to this offering.

Some of the statements under the captions "Prospectus summary," "Risk factors," "Use of proceeds," "Management's discussion and analysis of financial condition and results of operations" and "Business" and elsewhere in this prospectus are forward-looking statements. These forward-looking statements include, but are not limited to, statements about our plans, objectives, expectations and intentions and other statements contained in the prospectus that are not historical facts. When used in this prospectus, the words "anticipates," "believes," "continue," "could," "estimates," "expects," "intends," "may," "plans," "seeks," "should," "will" or "would" or the negative of these terms or similar expressions are generally intended to identify

forward-looking statements. Because these forward-looking statements involve risks and uncertainties, there are important factors that could cause actual results to differ materially from those expressed or implied by these forward-looking statements, including our plans, objectives, expectations and intentions and other factors discussed under "Risk factors."

USE OF PROCEEDS

We estimate that the net proceeds from the sale of the 9,000,000 shares of common stock that we are selling in the public offering will be approximately $74.3 million, or approximately $85.6 million if the underwriters' over-allotment option is exercised in full, based on an assumed initial public offering price of $9.00 per share and after deducting the estimated underwriting discount, commissions and estimated offering expenses payable by us. In addition, we expect to receive proceeds of approximately $10.0 million from the private placement of our common stock with Novartis concurrent with the closing of this offering.

We intend to use approximately 65% of the net proceeds for continued research and development activities, approximately 20% for general corporate purposes, approximately 15% for working capital and capital leasing obligations and the balance, if any, for financing possible acquisitions and investments in technology and for our facilities. We may also use a portion of the net proceeds to acquire or invest in businesses, products and technologies that are complementary to our own, although no acquisitions are planned or being negotiated as of the date of this prospectus, and no portion of the net proceeds has been allocated for any specific acquisition. Pending these uses, the net proceeds will be invested in investment-grade, interest-bearing securities.

The principal purposes of this offering are to increase our capitalization and financial flexibility, to provide a public market for our common stock and to facilitate access to public equity markets. As of the date of this prospectus, we cannot specify with certainty all of the particular uses for the net proceeds we will have upon completion of the public offering and the concurrent private placement. Accordingly, our management will have broad discretion in the application of net proceeds.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. Delaware law and our certificate of incorporation do not require our board of directors to declare dividends on our common stock. We currently intend to retain earnings, if any, to support the development of our business and do not anticipate paying cash dividends for the foreseeable future.

CAPITALIZATION

The following table sets forth our capitalization as of June 30, 2000:

- on an actual basis;
- on a pro forma basis to give effect to the automatic conversion of all outstanding shares of our convertible preferred stock upon the completion of this offering; and
- on a pro forma as adjusted basis to give effect to the sale of 9,000,000 shares of common stock by us in this public offering at an assumed price of $9.00 per share, less the estimated underwriting discounts, commissions and estimated offering expenses payable by us, and the sale of 1,111,111 shares of common stock in a private placement to Novartis concurrent with the closing of this initial public offering at an assumed price of $9.00 per share.

<TABLE>
<CAPTION>

	JUNE 30, 2000		
	(UNAUDITED)		
	ACTUAL	PRO FORMA	PRO FORMA AS ADJUSTED
	(IN THOUSANDS, EXCEPT SHARE AND PER SHARE DATA)		
<S>	<C>	<C>	<C>
Capital lease obligations, less current portion.....	$ 5,121	$ 5,121	$ 5,121
Stockholders' equity:			
Convertible preferred stock, $.001 par value; 26,750,000 authorized, 24,719,677 shares issued and outstanding, actual; none issued and outstanding pro forma and pro forma as adjusted.....	25	--	--
Common stock,$.001 par value; 37,500,000 shares authorized (100,000,000 shares pro forma); 4,428,552 shares issued and outstanding, actual; 29,148,229 shares issued and			

outstanding, pro forma and 39,259,340 shares issued and outstanding, pro forma as adjusted (1)	4	29	39
Additional paid-in capital	55,982	55,982	140,302
Deferred stock compensation	(5,333)	(5,333)	(5,333)
Accumulated deficit	(39,420)	(39,420)	(39,420)
Total stockholders' equity	11,258	11,258	95,588
Total capitalization	$ 16,379	$ 16,379	$100,709

</TABLE>

- ------------------------

(1) Excludes:

- 5,158,884 shares issuable upon the exercise of options outstanding as of June 30, 2000, at a weighted average exercise price of $1.58 per share;

- 540,038 shares issuable upon the exercise of warrants outstanding as of June 30, 2000, at a weighted average exercise price of $1.16 per share; and

- 2,445,064 additional shares available for future grant under our equity incentive plan, of which options to purchase 722,010 shares of common stock were granted through August 31, 2000; an additional 400,000 shares made available for future grant under our employee stock purchase plan; and 300,000 shares made available for future grant under our non-employee directors' stock option plan.

DILUTION

The pro forma net tangible book value on June 30, 2000, giving effect to the automatic conversion of all shares of preferred stock outstanding as of that date into shares of common stock upon the closing of this public offering was approximately $11.3 million, or $.39 per share. Pro forma net tangible book value per share represents the amount of our total tangible assets less total liabilities divided by the number of shares of common stock outstanding. Dilution in pro forma net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately afterwards. Assuming our sale of 9,000,000 shares of common stock offered by this prospectus at an assumed initial public offering price of $9.00 per share, after deducting estimated underwriting discounts and commissions and estimated offering expenses, and giving effect to the sale of 1,111,111 shares of common stock to Novartis concurrent with the closing of this initial public offering at an assumed price of $9.00 per share, our pro forma net tangible book value after this offering would have been approximately $95.6 million, or $2.43 per share. This represents an immediate decrease in net tangible book value of $6.57 per share to new investors purchasing shares of common stock in this offering. The following table illustrates this per share dilution:

<TABLE>

<S>	<C>	<C>
Assumed initial public offering price per share		$ 9.00
Pro forma net tangible book value per share as of June 30, 2000	$ .39	
Increase per share attributable to new investors	2.04	
Pro forma net tangible book value per share after this offering		2.43
Dilution per share to new investors		$ 6.57

</TABLE>

The following table summarizes, on a pro forma basis as of June 30, 2000, the differences between the total consideration paid and the average price per share paid by the existing stockholders and the purchasers of shares of common stock in this initial public offering and the concurrent private placement. We have assumed an initial public offering price of $9.00 per share and no exercise of the underwriters' over-allotment option, and we have not deducted estimated underwriting discounts and commissions and estimated offering expenses in our calculations.

<TABLE>
<CAPTION>

	SHARES PURCHASED		TOTAL CONSIDERATION		AVERAGE PRICE PER SHARE
	NUMBER	PERCENT	AMOUNT	PERCENT	
<S>	<C>	<C>	<C>	<C>	<C>
Existing investors	29,148,229	74.2%	$ 42,810,000	32.0%	$1.47
New investors	10,111,111	25.8	91,000,000	68.0	9.00

Total	39,259,340	100.0%	$133,810,000	100.0%

</TABLE>

The foregoing discussion and tables assume no exercise of any outstanding stock options or warrants at June 30, 2000. The exercise of all options and warrants outstanding as of June 30, 2000 having an exercise price less than the offering price would increase the dilutive effect to new investors to $6.72 per share.

SELECTED FINANCIAL DATA

The following selected financial data should be read in conjunction with the financial statements and the notes to such statements and "Management's discussion and analysis of financial condition and results of operations." The selected financial data in this section is not intended to replace the financial statements.

The statements of operations data for the years ended December 31, 1997, 1998 and 1999 and the balance sheet data as of December 31, 1998 and 1999 have been derived from our audited financial statements which have been audited by Ernst & Young LLP, our independent auditors and included elsewhere in this prospectus. The audited balance sheet data as of December 31, 1997 has been derived from our audited financial statements not included in this prospectus. The statements of operations data for the six months ended June 30, 1999 and 2000 and the balance sheet data as of June 30, 2000 have been derived from our unaudited financial statements included elsewhere in this prospectus. The statement of operations data for the period from inception (June 14, 1996) through December 31, 1996 and the balance sheet data as of December 31, 1996 are derived from our unaudited financial statements not included in this prospectus. The unaudited financial statements have been prepared on a basis consistent with our audited financial statements and include all adjustments, consisting only of normal recurring adjustments, we consider necessary for the fair presentation of the information. Historical results are not necessarily indicative of future results. See notes to the financial statements for an explanation of the method used to determine the number of shares used in computing pro forma basic and diluted net loss per share.

<TABLE>
<CAPTION>

	PERIOD FROM INCEPTION (JUNE 14, 1996) THROUGH DECEMBER 31,	FISCAL YEARS ENDED DECEMBER 31,			SIX MONTHS ENDED JUNE 30,	
	1996	1997	1998	1999	1999	2000
	(UNAUDITED)					(UNAUDITED)
<S>	<C>	<C>	<C>	<C>	<C>	<C>
STATEMENTS OF OPERATIONS DATA:		(IN THOUSANDS, EXCEPT PER SHARE AMOUNTS)				
Contract revenues from collaborations	$ --	$ --	$ 28	$ 8,984	$ 3,069	$ 6,797
Costs and expenses:						
Research and development (see Note A)	--	4,568	8,305	17,112	6,830	14,636
General and administrative (see Note A)	133	1,033	2,217	3,952	1,708	2,994
Total costs and expenses	133	5,601	10,522	21,064	8,538	17,630
Loss from operations	(133)	(5,601)	(10,494)	(12,080)	(5,469)	(10,833)
Interest income (expense), net	--	85	(110)	(286)	12	32
Net loss	$ (133)	$(5,516)	$(10,604)	$(12,366)	$(5,457)	$(10,801)

</TABLE>

Net loss per share, basic and diluted.....	$ (.12)	$ (2.20)	$ (4.01)	$ (4.39)	$ (2.02)
$ (2.60)					
	======	=======	========	========	=======
========					
Weighted average shares used in computing net loss per share, basic and diluted.....	1,089	2,512	2,643	2,818	2,703
4,162					
Pro forma net loss per share, basic and diluted....				$ (.52)	
$ (.38)					
				========	
========					
Weighted average shares used in computing pro forma net loss per share, basic and diluted.....				23,996	
28,393					
Note A:					
Includes charges for stock-based compensation as follows:					
Research and development.....	$ --	$ --	$ 6	$ 2,321	$ 163
$ 4,245					
General and administrative.....	$ --	$ --	$ --	$ 254	$ 41
$ 396					

	AS OF DECEMBER 31,				AS OF JUNE 30,
	1996	1997	1998	1999	2000
	(UNAUDITED)				(UNAUDITED)
<S>	<C>	<C>	<C>	<C>	<C>
			(IN THOUSANDS)		
BALANCE SHEET DATA:					
Cash and cash equivalents.....	$ 2	$9,144	$ 9,493	$ 5,836	$15,694
Working capital (deficit).....	(71)	8,109	4,547	(990)	8,580
Total assets.....	2	11,330	12,956	17,169	25,516
Capital lease obligations, less current portion....	--	1,172	1,652	5,478	5,121
Deferred stock compensation.....	--	--	--	(5,814)	(5,333)
Accumulated deficit.....	(133)	(5,649)	(16,253)	(28,619)	(39,420)
Total stockholders' equity/(net capital deficiency).....	(71)	8,819	5,445	756	11,258

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

THE FOLLOWING DISCUSSION AND ANALYSIS SHOULD BE READ WITH "SUMMARY FINANCIAL DATA" AND OUR FINANCIAL STATEMENTS AND NOTES INCLUDED ELSEWHERE IN THIS PROSPECTUS. THE DISCUSSION IN THIS PROSPECTUS CONTAINS FORWARD-LOOKING STATEMENTS THAT INVOLVE RISKS AND UNCERTAINTIES, SUCH AS STATEMENTS OF OUR PLANS, OBJECTIVES, EXPECTATIONS AND INTENTIONS. THE CAUTIONARY STATEMENTS MADE IN THIS PROSPECTUS SHOULD BE READ AS APPLYING TO ALL RELATED FORWARD-LOOKING STATEMENTS WHEREVER THEY APPEAR IN THIS PROSPECTUS. OUR ACTUAL RESULTS COULD DIFFER MATERIALLY FROM THOSE DISCUSSED HERE. FACTORS THAT COULD CAUSE OR CONTRIBUTE TO THESE DIFFERENCES INCLUDE THOSE DISCUSSED IN "RISK FACTORS," AS WELL AS THOSE DISCUSSED ELSEWHERE IN THIS PROSPECTUS.

OVERVIEW

We use post-genomics combinatorial biology technology to discover novel drug targets. Our technology provides a new and rapid way to find novel drug targets and to validate the role of those targets in disease. We intend to develop a portfolio of novel drug candidates and commercialize the resulting drug products in partnership with corporate collaborators. We have incurred net losses since inception and expect to incur substantial and increasing losses for the next several years as we expand our research and development activities and move our pre-clinical drug candidates into later stages of development. To date, we have funded our operations primarily through the sale of equity securities, non-equity payments from collaborative partners and capital asset lease financings. We received our first funding from our collaborative partners in December 1998. Including both research funding and equity investments, we received an aggregate of $6.5 million, $14.9 million and $7.7 million in 1998, 1999 and the first six months of 2000, respectively, from our collaborative partners. As of June 30, 2000, our accumulated deficit was approximately $39.4 million.

We expect our sources of revenue for the next several years to consist primarily of payments under our current and future corporate collaborations. Under these arrangements, sources of revenue may include up-front payments, funded research, milestone payments and royalties. The process of carrying out our research programs for our collaborative partners and the development of our own non-partnered products to the later stages of development will require significant additional research and development expenditures including

preclinical testing and clinical trials. These activities, together with our general and administrative expenses, are expected to result in substantial operating losses for the foreseeable future. We will not receive product revenue unless we or our collaborative partners complete clinical trials, obtain regulatory approval and successfully commercialize one or more of our products.

To date, we have entered into three collaborations with major pharmaceutical companies that are currently contributing to our revenues. A summary of these partnerships is as follows:

<TABLE>
<CAPTION>

PARTNER	RESEARCH PROGRAM	COMMENCEMENT DATE
<S>	<C>	<C>
Janssen Pharmaceutica	Tumor Growth--Cell Cycle Inhibition	December 4, 1998
Pfizer	Asthma/Allergies--IgE Production in B Cells	January 31, 1999
Novartis	Transplant Rejection--T Cell Activation	May 26, 1999
	Autoimmunity Disease--B Cell Activation	August 1, 1999
	Pulmonary Lung Inflammation (conducted at Novartis)	January 1, 2000

</TABLE>

Under the terms of the existing collaborations identified above, our partners have agreed to provide future research funding up to approximately $30.0 million over the next four years, $18.0 million of which is subject to possible cancellation. In addition, we may receive additional payments upon the achievement of specific research and development milestones and royalties upon commercialization of any products.

In order to maintain and increase proceeds from collaborations, we are addressing several alternatives, including the exploration of new opportunities with existing and new potential collaborators. All of our partnerships to date have generally focused on the early stages of drug discovery, specifically

target discovery and validation. We expect to continue to engage in collaborations focused on the early stages of drug discovery. In addition, we currently anticipate that we will self-fund some of our own research programs to later stages of development prior to partnering with collaborative partners. Therefore, it is expected that any future collaborative partnerships will have an expanded focus and could include cell pathway mapping, high throughput screening, combinatorial chemistry and/or pre-clinical evaluations. For some programs, we may also seek to enter into collaborations for the development of compounds that we have discovered. The timing, the amount of funds received and the scope of any new collaboration are uncertain and any compound collaboration will depend on the successful progress of clinical trials. New, expanded or larger collaborations will also be necessary to offset any decrease in proceeds as collaborations come to the end of their terms. Specifically, our collaboration with Pfizer is a two-year agreement terminating on January 31, 2001 and our collaboration with Janssen Pharmaceutica is a three-year agreement terminating on December 31, 2001. Our Novartis programs are five-year agreements terminating in 2004 and 2005. Although all of our agreements provide for potential extension, we do not expect that our collaboration with Pfizer will be renewed and we cannot ensure that our collaborative partners will exercise these extension rights. As our collaborations reach termination, our partners and we may evaluate the status of the collaboration and, if appropriate, seek to extend the collaboration agreement or negotiate alternative terms.

We recognize revenues from our research collaboration agreements as earned upon the achievement of performance requirements of the agreements. In addition, these agreements provide for research funding for a specified number of full time researchers working on their associated projects. Payments received that are related to future performance are deferred and recognized as revenue as the related work is performed. As of June 30, 2000, we had deferred revenues of approximately $3.3 million.

DEFERRED STOCK COMPENSATION

We recorded deferred stock compensation with respect to options granted to employees of approximately $7.1 million in the year ended December 31, 1999 and $1.5 million for the six months ended June 30, 2000, representing the difference between the deemed fair value of our common stock for financial reporting purposes on the date these options were granted and the exercise price. These amounts has been reflected as components of stockholders' equity and the deferred expense is being amortized to operations over the vesting period of the options, generally four to five years, using the graded vesting method. We amortized deferred stock compensation of $1.3 million in 1999, with $1.0 million recorded as a research and development expense and $.3 million as a general and administration expense. In the six months ended June 30, 2000, we amortized deferred stock compensation of $2.0 million, with $1.6 million recorded as research and development expense and $.4 million as a general and administration expense. At June 30, 2000, we had a total of $5.3 million remaining to be amortized over the vesting periods of the stock options. We anticipate that additional deferred stock compensation will be recorded for options granted after June 30, 2000 and expect to record approximately

$1.2 million for stock options granted from July 1, 2000 through August 31, 2000. For the year ending December 31, 2000, the total amortization of deferred stock compensation is expected to be approximately $3.8 million. We also expect to record deferred stock compensation for options granted from July 1, 2000 through August 31, 2000 to new hires who will commence employment with the Company at a later date. The deferred stock compensation will be recorded based on the fair value of our common stock at the date employment commences and amortized in accordance with our policy.

RESULTS OF OPERATIONS FOR THE SIX MONTHS ENDED JUNE 30, 1999 AND 2000

REVENUES. Collaborative research and development revenues were $6.8 million for the six months ended June 30, 2000, compared with $3.1 million for the six months ended June 30, 1999. In the first six months of 2000, revenues were earned from technology access fees and research support from all collaborations, including Janssen Pharmaceutica, Pfizer and three Novartis projects. Revenues for the first

six months of 1999 consisted primarily of revenues from the Janssen Pharmaceutica and Pfizer collaborations, with Novartis contributing an insignificant amount of revenue since the agreement was signed in late May 1999.

RESEARCH AND DEVELOPMENT EXPENSES. Research and development expenses were $14.6 million for the six months ended June 30, 2000, compared with $6.8 million for the six months ended June 30, 1999, an increase of $7.8 million. This increase was primarily attributable to increases in employee costs as our science headcount was 58 at June 30, 1999 and 78 individuals at June 30, 2000 and also the higher occupancy costs associated with the new building in South San Francisco, California, which we occupied from March 1999. In addition, the research and development expenses included $4.2 million and $.2 million in stock compensation expenses in the six months ended June 30, 2000 and 1999, respectively.

GENERAL AND ADMINISTRATIVE EXPENSES. General and administrative expenses were $3.0 million for the six months ended June 30, 2000, compared with $1.7 million for the six months ended June 30, 1999, an increase of $1.3 million. This increase was primarily attributable to higher employee and occupancy costs. General and administrative expenses included $396,000 and $41,000 in stock compensation expenses in the six months ended June 30, 2000 and 1999, respectively.

NET INTEREST INCOME. Net interest income was $32,000 for the six months ended June 30, 2000, compared with a net interest income of $12,000 for the corresponding period in 1999 due mainly to higher cash balances in 2000 from the sale of the Series E preferred stock.

YEARS ENDED DECEMBER 31, 1999, 1998 AND 1997

REVENUES. Contract revenues from collaborations were $9.0 million in 1999 compared to $28,000 in 1998. Revenues in 1998 and 1999 were due to the initiation of three of our corporate collaborations. The collaboration with Janssen Pharmaceutica was signed in December 1998 with research support beginning on January 1, 1999 while the Pfizer collaboration was initiated on January 31, 1999. The Novartis collaboration, which was signed on May 26, 1999, consists of five research programs. Of these five programs, one was started on May 26, 1999 with a second program initiated on August 1, 1999. We expect contract revenue from collaborations to be a significant component of our total revenues for the foreseeable future.

RESEARCH AND DEVELOPMENT. Research and development expenses increased to $17.1 million in 1999 from $8.3 million in 1998 and $4.6 million in 1997, an increase of $8.8 million and $3.7 million, respectively. These increases are primarily attributable to increases in employee costs as our science headcount increased to 66 individuals from 41 in 1998 and 22 in 1997 and the higher occupancy costs associated with our new building in South San Francisco, California, which we occupied in March 1999. Research and development expenses in 1999 included $1.0 million related to the amortization of deferred stock compensation in connection with options granted to employees and $1.3 million related to compensation on options granted to consultants and the issuance of stock for consultant services. We expect research and development expenses to increase in future periods in connection with the addition of new collaborative partner research programs. In addition, we anticipate research and development expenses will increase with the advancement of our non-partnered research programs into later stages of development.

GENERAL AND ADMINISTRATIVE EXPENSES. General and administrative expenses were $4.0 million in 1999, compared with $2.2 million in 1998 and $1.0 million in 1997, an increase of $1.8 million and $1.2 million, respectively. These increases were primarily attributable to higher employee costs, infrastructure costs to support the growing research and development activities and increased occupancy costs. The general and administrative expenses in 1999 included $.3 million related to the amortization of deferred stock in connection with options granted to employees. We expect that general and administrative expenses

will increase in the future to support the continued growth of our research and development efforts and to accommodate the new demands associated with operating as a public company.

NET INTEREST EXPENSE. Net interest expense was $286,000 in 1999, compared with a net interest expense of $110,000 in 1998 and net interest income of $85,000 in 1997. Interest income results from our interest bearing balances while interest expense is the result of our debt associated with fixed asset purchases.

LIQUIDITY AND CAPITAL RESOURCES

We have financed our operations from inception primarily through sales of preferred stock, contract payments payable to us under our collaboration agreements and equipment financing arrangements. As of June 30, 2000, we had received $42.8 million from the sale of equity securities, including $9.0 million from collaborators, and received $19.1 million in research funding from collaborators. In addition, as of June 30, 2000, we had financed through leases and loans the purchase of equipment and leasehold improvements totaling approximately $11.0 million.

As of June 30, 2000, we had $15.7 million in cash and cash equivalents as compared to $5.8 million as of December 31, 1999, an increase in cash balances of $9.9 million. This increase in cash balances is derived principally from the sale of our Series E preferred stock, from which we received net proceeds of $15.1 million, offset by our usage of $4.0 million for the funding of operations and the investment of $1.6 million in capital equipment and leasehold improvements. We made $1.1 million in payments associated with our equipment financing arrangements, offset by the receipt of $1.1 million from our equipment financing arrangements and the receipt of $15.5 million in net proceeds from equity securities.

As of June 30, 2000, we had $7.6 million in capitalized lease obligations in association with our financed purchase of equipment and leasehold improvements. These obligations are secured by the equipment financed, bear interest rates in a range of 7% to 15% and are due in monthly installments through 2004. Under the terms of our three equipment financing agreements, two of these have balloon payments at the end of each loan term, while the other agreement allows us to purchase the assets financed at the fair market value or 20% of the original acquisition cost at the end of the financing term. As of June 30, 2000, we completely utilized our existing equipment financing agreements and on August 22, 2000, we completed negotiations for a new equipment financing agreement that could provide an incremental $5.0 million of equipment financing proceeds to be utilized over the next twelve to eighteen months, of which the first equipment financing of $1.1 million was utilized in August, 2000. Under the terms of this new lease, payments are due in monthly installments over four years and bear interest rates of approximately 11%.

On February 3, 2000, we received approximately $15.1 million, net of issuance costs, in a private placement in which we sold 2,508,330 shares of Series E preferred stock at $6.00 per share. In addition, in September 2000, we exercised our right within the Novartis collaboration agreement to have Novartis purchase shares of our common stock in a private placement concurrent with this initial public offering at the initial public offering price. We anticipate receiving an additional $10.0 million in proceeds from the concurrent private placement to Novartis. We believe our existing cash resources, including the proceeds from the private placement, plus the proceeds of this public offering and anticipated proceeds from corporate collaborations will be sufficient to satisfy our anticipated cash requirements through at least 24 months. Our future capital uses and requirements depend on numerous forward-looking factors. These factors include and are not limited to the following:

- our ability to maintain our existing collaboration partnerships;

- our ability to establish and the scope of our new collaborations;

- the progress and number of research programs carried out at Rigel;

- our ability to meet the milestones identified in our collaborative agreements which trigger payments;

- the progress and success of preclinical and clinical trials of our drug candidates;

- the costs and timing of obtaining, enforcing and defending our patent and intellectual rights;

- the costs and timing of regulatory approvals; and

- expenses associated with unforeseen litigation.

In addition, we are constantly reviewing potential opportunities to expand our technologies or add to our portfolio of drug candidates. In the future, we

may need further capital in order to acquire or invest in technologies, products or businesses. For the next several years, we do not expect the cash generated from our operations to generate the amount of cash required by our future cash needs. We expect to finance future cash needs through the sale of equity securities, strategic collaborations and debt financing. We cannot assure you that additional financing or collaboration and licensing arrangements will be available when needed or that, if available, this financing will be obtained on terms favorable to us or our stockholders. Insufficient funds may require us to delay, scale back or eliminate some or all of our research or development programs, to lose rights under existing licenses or to relinquish greater or all rights to product candidates at an earlier stage of development or on less favorable terms than we would otherwise choose or may adversely affect our ability to operate as a going concern. If additional funds are obtained by issuing equity securities, substantial dilution to existing stockholders may result.

QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive from our investments without significantly increasing risk. Some of the securities that we invest in may have market risk. This means that a change in prevailing interest rates may cause the principal amount of the investment to fluctuate. For example, if we hold a security that was issued with a fixed interest rate at the then-prevailing rate and the prevailing interest rate later rises, the principal amount of our investment will decline. To minimize this risk in the future, we intend to maintain our portfolio of cash equivalents and short-term investments in a variety of securities, including commercial paper, money market funds, government and non-government debt securities. In 1998, 1999 and the six months ended June 30, 2000, we maintained an investment portfolio primarily in depository accounts. Due to the short-term nature of these investments, we believe we have no material exposure to interest rate risk arising from our investments. Therefore, no quantitative tabular disclosure is provided.

We have operated primarily in the United States, and all funding activities with our collaborators to date have been made in U.S. dollars. Accordingly, we have not had any exposure to foreign currency rate fluctuations.

BUSINESS

OVERVIEW

We use post-genomics combinatorial biology technology to discover novel drug targets. In only three and one-half years of research using our technology, we have succeeded in identifying 22 new drug targets in eight of our nine programs and have generated compounds in five programs, including compounds which are candidates for preclinical testing in two of these programs. We currently have programs in asthma/allergy, autoimmunity, transplant rejection, rheumatoid arthritis, inflammatory bowel disease and cancerous tumor growth. We have a collaboration with Pfizer and multi-year collaborations with Cell Genesys, Janssen Pharmaceutica and Novartis. In addition, we have collaborated with Neurocrine in order to obtain rights to a library of small chemical compounds.

BACKGROUND

GENERAL

We were incorporated in the State of Delaware on June 14, 1996. Our results of operations from June 14, 1996 to December 31, 1996 were immaterial. We matured from a development stage to an operating company in 1998. The company has funded its operations primarily through the sale of private equity securities, payments from corporate collaborators and capital asset lease financings. We have no subsidiaries.

PHARMACEUTICAL INDUSTRY NEED FOR NEW DRUGS AND NOVEL TARGETS

In order to sustain growth, each major pharmaceutical company needs to bring approximately two or more new drugs to market each year. However, it is currently estimated that, using traditional drug discovery and development methodologies, each major pharmaceutical company is bringing to market, on average, less than one new drug per year. As a result, major pharmaceutical companies have a discovery and product pipeline gap. In addition, we believe this demand for new products will be increased by the expiration in coming years of patents on numerous significant revenue-generating drugs.

We believe that several thousand of the more than 100,000 genes in the human genome will provide potential drug targets directed at specific diseases. Despite this potential, researchers have only identified and validated approximately 500 distinct targets for existing drug interventions which serve as the basis for many pharmaceutical products today. We feel that the existing, relatively small, pool of potential targets limits pharmaceutical companies' opportunities to develop new drug candidates to satisfy their growth objectives. Moreover, we believe this situation creates a critical need for tools directed at novel ways to expand the pool of targets by rapidly identifying and

successfully validating new targets which lead to new chemical entities.

TRADITIONAL DRUG DISCOVERY

The traditional drug discovery process involves testing or screening compounds in disease models. The process is often undertaken with little knowledge of the intracellular processes underlying the disease or the specific drug target within the cell. Consequently, it is necessary to screen a very large number of arbitrarily-selected compounds in order to obtain a desired change in a disease model. While this approach sometimes successfully produces drugs, it has a number of disadvantages:

- INEFFICIENCY: it is labor intensive, time consuming and inefficient at identifying and validating targets;

- LACK OF PRODUCTIVITY: it results in relatively few new drug candidates, or "hits";

- LACK OF INFORMATION: it produces limited information about the intracellular processes or targets to guide target selection and subsequent drug development; and

- RISK OF SIDE EFFECTS: it often produces drug candidates with a high risk of serious side effects, including toxicity.

SUBSEQUENT BIOLOGICAL ADVANCES AND GENOMICS

Beginning in the mid 1970s, pharmaceutical companies began to use a growing knowledge of cellular and molecular biology to enlarge their understanding of biochemical interactions within and between cells in order to understand the cellular basis for disease processes. For example, researchers equipped with a more thorough understanding of cellular mechanisms relating to blood pressure regulation were able to identify proteins called angiotensin converting enzymes (ACE) which regulate molecules causing high blood pressure. By identifying compounds that act as ACE inhibitors, the researchers developed a family of highly specific drugs that lower blood pressure without causing serious side effects.

More recently, pharmaceutical companies have begun to look at the genetic basis for disease. For example, the Human Genome Project was undertaken to identify the DNA sequence of all the genes in the human genome, with the hope that knowledge of the human genome would enable a comprehensive understanding of the molecular causes of all diseases, and therefore provide a source of targets for drug discovery. However, merely developing sequence data with respect to genes does not, on its own, provide information about the cellular function of the proteins encoded by the genes expressed in a particular tissue at a particular time under particular disease circumstances. In addition, it fails to tell us which proteins might make useful targets for compound screening to identify drug candidates to modulate any of these functions. With more than 100,000 genes in the human genome, the number of possible combinations of expressed proteins in a cell and the number of possible interactions of those proteins produce a volume of information which often obscures rather than illuminates the functional role of any particular gene in a disease process.

Later efforts to link genes to disease, or functional genomics, have focused on the genes that are responsible for changes in the behavior of cells under disease conditions. However, the functional connection between particular genes and their expressed proteins on the one hand, and cellular behavior seen in disease conditions on the other hand, has remained unknown in the majority of diseases. For this reason, pharmaceutical companies have sought better means to identify the genes that are important to cellular behavior and to understand their role in causing or preventing disease. Whether through gene sequencing or functional genomics, understanding the functional role of a gene is critical to understanding, identifying and validating a gene's expressed protein as a target for compound screening. We believe that there remains a critical need for research methods that will be able to utilize the information currently available to identify protein targets quickly and systematically, with increased probability of discovering new drug candidates.

ROLE OF TARGET VALIDATION

The identification of intracellular protein targets is an important step in the process of identifying potential drugs. Most drugs are discovered today by screening collections of libraries of chemical compounds against protein targets which are part of signaling, or information-transmitting, pathways within cells. These signaling pathways participate in the regulation of cell behavior in both normal and diseased cells. However, drug discovery and development often occurs without first validating the drug target and mechanism of action. If pharmaceutical companies were to validate a target's role in a disease at an early stage, they would reduce risks involved in the drug development process, such as the pursuit of unsuccessful discovery pathways, regulatory delay and drug side effects.

A target is regarded as validated if a causal link is established between an

intracellular protein target and a cellular response important in a disease process. Each drug discovery company has its own standards for deciding whether a target has been sufficiently validated.

OUR SOLUTION

Our drug target discovery process bypasses the need to know the identity or sequence of the genes. We have developed two core technologies which we believe provide us with an enhanced ability to simultaneously identify and initially validate new drug targets for further development.

Our technologies are designed to identify protein targets for compound screening and validate the role of those targets in the disease process. Unlike genomics-based approaches, which begin by identifying genes and then search for their functions, our approach identifies proteins that are demonstrated to have an important role in a disease pathway. By understanding the disease pathway, we attempt to avoid studying genes that will not make good drug targets and focus only on the sub-set of expressed proteins of genes that we believe are specifically implicated in the disease process.

We begin by developing assays which model the key events in a disease process at the cellular level. We then efficiently search hundreds of millions of cells to identify potential protein targets. In addition, we identify the proteins involved in the intracellular process and prepare a map of their interactions, thus giving us a comprehensive picture of the intracellular disease pathway. We believe that our approach has a number of advantages:

- IMPROVED TARGET IDENTIFICATION: it focuses only on the sub-set of expressed proteins of genes believed to be specifically implicated in the disease process;

- RAPID VALIDATION OF PROTEIN TARGETS: it produces validated protein targets more quickly because it uses key events in the disease process as the basis to design the functional, disease-based screen;

- IMPROVED DISEASE PATHWAY MAPPING: it produces a comprehensive map of the intracellular disease pathway enabling the identification of a larger number of potential protein targets;

- BETTER INFORMED TARGET SELECTION: it provides a variety of different types of targets and information concerning the role each plays to better select targets more susceptible to pharmaceutical intervention;

- MORE EFFICIENT COMPOUND SCREENING: it increases the probability and speed that compound screening will identify "hits" because it provides more detailed knowledge of the target which can be used to guide the design of the compound screen; and

- RISK REDUCTION: it may reduce the risk of failure in the drug development process due to serious side effects, including toxicity or other reasons, by selecting only targets that are specific to the disease in question and which have no apparent role in other cell types or signaling pathways.

Because of the very large number of cells and proteins employed, our technology is labor intensive. The complexity of our technology requires a high degree of skill and diligence to perform successfully. In addition, successful application of our technology depends on a highly diverse collection of proteins to test in cells. We believe we have been able to and will continue to meet these challenges successfully. Although one or more other companies may utilize technologies similar to certain aspects of our technology, we are unaware of any other company which employs the same combination of technologies as we do.

TECHNOLOGY

Our retroviral and pathway mapping technologies enable us to identify and validate new protein targets and establish a map of the intracellular proteins that define a specific signaling pathway controlling cellular responses. We believe that, together, these technologies allow for rapid pathway mapping of complex biological processes and increase our ability to identify targets for drug discovery.

Our retroviral technology introduces up to 100 million different peptides or proteins into an equal number of normal or diseased cells. Each retrovirus delivers a specific gene into an individual cell, causing the cell to produce a specific protein. Then, we stimulate the cells in a manner known to produce a

disease-like behavioral response or phenotype of the disease process. Once in the cell, the expressed protein interacts with potential protein targets in the cell. Then, we sort the cells at a rate of up to 60,000 cells/second to collect data on up to five different parameters which means that a sort of 100 million cells can be completed in approximately half an hour. By analyzing the approximately 500 million resulting data points, we can rapidly identify those few cells containing an expressed protein that has interacted with a protein

target in a way that causes the cell to change its behavior from diseased back to normal. Using this method we believe that we can identify the relatively few targets that are validated in the context of a disease-specific cellular response.

Our pathway mapping technology identifies specific proteins that bind with other proteins that are known to be part of a signaling pathway, either because we identified them using our retroviral technology or because the proteins have been described in the scientific literature. This pathway mapping technology is directed at:

- mapping an entire protein-protein intracellular functional pathway in disease relevant cells;

- finding new proteins interacting with other new and known proteins; and

- eliminating potential targets rapidly because they interact with multiple signaling pathways, thus identifying the protein as a less desirable target.

Using our pathway mapping technology, we split a protein that gives a detectable signal (reporter protein), such as fluorescence, into two inactive parts. One part of the reporter protein is fused with a specific protein known to be involved in a signaling disease-relevant pathway (bait protein). Multiple copies of the other part of the reporter protein are fused one by one with all the proteins known to be present in the cell type being studied (library protein). When the bait protein binds to a specific library protein, the two parts of the reporter protein reunite and become active again, thereby generating a detectable signal. We employ an improved version of the two hybrid protein interaction method in yeast cells. In addition, we have developed a patented method of employing the two hybrid protein interaction technology in mammalian cells. Mammalian cells offer the opportunity to monitor protein-protein interactions in a potentially more relevant cellular environment.

We also use this pathway mapping technology to screen identified protein targets against a library of peptides in order to identify each active interaction site on the target. This information is useful in directing our chemistry efforts to identify compounds specifically designed to bind to the interaction site on the target.

TARGET VALIDATION

The first step of our target validation occurs when we use our retroviral technology to identify targets. We design a screen that reflects a key event in a disease process so that when one of our proteins changes the behavior of a specific cell, this indicates a causal relationship between the protein-target interaction and the specific disease response. This approach saves time and enhances the probability that those targets which are identified and pursued are disease relevant. It also tells us that the protein interacts with a functional site on the target since the interaction results in a change in the behavior of the cell. We further validate the function of specific targets by:

- using technology to knock out the target from specific cells and seeing if the loss of the target from the cell alters the cell's responses to disease-causing stimuli;

- altering the structure of the target in order to identify which part of the target is functionally important; and

- using peptides that attach to specific sites on the target to change the way the target works inside the cell.

OUR DISCOVERY PROGRESS: 1997 - 2000

Since 1997, we have detected more than 500 million protein-protein interactions in cells. We have also discovered more than 10,000 signaling pathway members which modify cellular function. We have mapped the protein interactions of over 150 disease modifying protein targets in nine disease relevant pathways. We have identified 22 new targets in our programs suitable for screening compounds for drugs: asthma/ allergy, autoimmunity, transplant rejection, rheumatoid arthritis (both E-3 ubiquitin ligase and tumor necrosis factor (TNF) pathway), inflammatory bowel disease and cancerous tumor growth (both cell cycle inhibition and E-3 ubiquitin ligase). We have identified small molecule compounds in five of our programs, including compounds which are candidates for preclinical testing in two of these programs.

[GRAPHIC]

OTHER TECHNOLOGIES

Our drug discovery technologies utilize the following additional technologies:

HIGH THROUGHPUT COMPOUND SCREENING

Using our cell sorter system, we conduct screening of small molecule compounds in the same cell-based disease-specific screens that we use to identify the protein targets. This enables us to screen thousands of compounds in a matter of a few hours, while simultaneously examining multiple physiological parameters. In addition, we have established conventional high throughput screens of small molecule compounds using biochemical methods similar to those widely used in the biotechnology and pharmaceutical industry. We have a library of approximately 135,000 synthetic small molecule compounds having highly diverse molecular structures for our compound screening activities.

We select for compound screening only those protein drug targets we judge to meet several criteria:

- the target's causal relationship to the disease of interest is established;

- the target's activity is determined to be specific to the disease of interest;

- the target is of a protein type, such as an enzyme, for which there is experience indicating that intervention by a synthetic small molecule compound would be an effective therapeutic; and

- the target is novel and provides us freedom of action to pursue drug discovery without interference from the rights of third parties.

PROTEOMICS

Our proteomics program is an integral part of our target discovery and validation effort. In contrast to our retroviral and pathway mapping technologies which can be used to find single protein-protein interactions, proteomics techniques can be used to find protein complexes comprised of several protein targets and to study protein-protein interactions in order to map active interaction sites on potential protein targets. To this end, we believe our protein chemistry group uses the most advanced proteomic technologies, including high resolution two dimensional gel electrophoresis in conjunction with in-gel tryptic digests followed by mass spectrometry, in order to identify specific drug targets.

MEDICINAL AND COMBINATORIAL CHEMISTRIES

Our medicinal chemistry group carries out traditional structure-activity relationship studies of potential lead compounds and makes improvements to those compounds by utilizing chemistry techniques to synthesize new analogs of a lead compound with improved properties. Our chemistry group synthesizes compounds incorporating desirable molecular features.

OUR STRATEGY

Our strategy is to develop a large portfolio of drug candidates that may be developed into small molecule therapeutics. We believe that producing a portfolio of many drug candidates and working in conjunction with pharmaceutical companies to further develop the candidates greatly increases our probability of commercial success. By utilizing our technology to rapidly discover and validate new targets and drug candidates that regulate them, we believe that we are well positioned to help fill the product pipeline gap of major pharmaceutical companies.

The key elements of our scientific and business strategy are to:

- expand, enhance and protect our technology;

- focus on diseases that represent large medical markets with significant populations that are currently under served;

- structure corporate partnering agreements to permit multiple collaborations in each disease area by focusing on disease pathways and targets;

- establish strategic collaborations with pharmaceutical and biotechnology companies to enhance product development and commercialization and to partner our future research programs in the later stages of drug development; and

- develop small molecule drugs, which can be delivered to intracellular targets.

PRODUCT DEVELOPMENT

We believe that, with a steadily aging population, the main focus of medicine in the United States and other developed countries is shifting to a

greater emphasis on the prevention and treatment of chronic diseases such as asthma and rheumatoid arthritis. The parallel trends of the increasing knowledge of drug targets and the increasing incidence of the diseases treated with small molecule compounds allow us to exploit our technology for large and fast growing segments of the pharmaceutical marketplace on a worldwide basis. Our programs address asthma/allergy, autoimmunity, transplant rejection, rheumatoid arthritis, inflammatory bowel disease affecting the immune system as well as cancerous tumor growth. These programs offer potential opportunities to develop drugs for many therapeutic indications. We believe that there are significant unmet medical and quality-of-life needs for these diseases that represent large commercial markets.

The following table summarizes key information in nine programs we are conducting at Rigel that focus on specific disease mechanisms:

<TABLE>
<CAPTION>

DISORDER/DISEASE	MECHANISM	STATUS	KEY ACHIEVEMENTS	COLLABORATIVE PARTNER
<S>	<C>	<C>	<C>	<C>
IMMUNE DISORDERS				
Asthma/allergy	IgE receptor pathway on mast cells	Preclinical development(1)	- Testing in animal models underway - Preclinical candidate compounds identified - Cell based high throughput screening (HTS) underway - Protein interaction pathway map established - Novel drug targets identified and validated	None
	IgE production in B cells	Target screening(2)	- Target screening underway	Pfizer
	IgE production in B cells	Compound screening(3)	- Compounds identified(5) - HTS underway(5) - Protein interaction pathway map established(5) - Novel drug targets identified and validated(5)	None
Autoimmunity and transplant rejection	B cell activation	Target validation(4)	- HTS underway - Protein interaction pathway map established - Novel drug targets identified	Novartis
	T cell activation	Target validation(4)	- HTS underway - Protein interaction pathway map established - Novel drug targets identified	Novartis
Rheumatoid arthritis and inflammatory bowel disease	E-3 ubiquitin ligase	Compound screening(3)	- Compounds identified - HTS underway - Novel drug targets identified and validated	None
	Selected TNF pathway targets	Target validation(4)	- Protein interaction pathway map established	None

</TABLE>

			- Novel drug targets identified	

<CAPTION>
CANCER

Tumor growth	Cell cycle inhibition	Compound screening(3)	- HTS underway - Protein interaction pathway map established - Novel drug targets identified and validated	Janssen Pharmaceutica
	E-3 ubiquitin ligase	Compound screening(3)	- Preclinical candidate compound identified - HTS underway - Novel drug targets identified and validated	None
	Angiogenesis	Target screening(2)	- HTS underway - Novel drug targets identified	Cell Genesys

</TABLE>

(1) "Preclinical development": Pharmacology and toxicology testing in animal models to gather data necessary to comply with applicable regulatory protocols prior to submission of an Investigational New Drug application to the FDA.

(2) "Target screening": Disease modeled screening in cells using our post-genomics combinatorial biology technology.

(3) "Compound screening": Screening of small molecule compounds in biochemical and cell based assays to identify a compound which binds to a functionally active site of a validated target.

(4) "Target validation": Testing to establish a causal link between an intracellular protein target and a cellular response important in a disease process.

(5) These key achievements occurred not as part of the Pfizer collaboration, but through our own separate research efforts.

IMMUNE DISORDERS

Many diseases and disorders result from defects in the immune system. Over 50 million people in the United States suffered from allergic and asthmatic disorders in 1999. Anti-asthmatic and allergy relief medications exceeded $5 billion in worldwide sales in 1997 and have been growing at a 5% annual growth rate. In 1999, another 3 million to 5 million patients in the United States were treated for other immune disorders. We currently have six programs in immunology focused on asthma/allergy (two programs), autoimmunity, transplant rejection, rheumatoid arthritis and inflammatory bowel disease and three programs in cancer focused on tumor growth.

ASTHMA/ALLERGY

IGE RECEPTOR ON MAST CELLS. The goal of this program is to identify compounds that inhibit the secretion of inflammatory factors resulting from IgE binding to its receptor on mast cells. IgE is one of several immunoglobulins produced by the body's immune system. Currently, we have identified preclinical candidate compounds. Preliminary studies demonstrate that these compounds inhibit the ability of IgE to activate its receptor on mast cells. There is evidence in animal models and early clinical studies that blocking IgE from binding to mast cells can reduce allergic symptoms in multiple species, including humans. However, most programs in development today are intravenous therapeutic antibodies. We

believe that small molecule inhibitors of IgE signaling pathways could play an important role in treatment of such chronic disorders.

IGE PRODUCTION IN B CELLS. In this program, we have been working with our partner, Pfizer, since January 1999 to identify intracellular drug targets that control the production of IgE in B cells. We have identified, not as part of the Pfizer collaboration, but separately through our own research efforts, a protein target that appears to regulate a key event in this pathway that leads to allergic and asthmatic symptoms and a compound in this program.

AUTOIMMUNITY AND TRANSPLANT REJECTION

Autoimmunity disorders and organ transplant rejection are the result of inappropriate activation of the immune system. Most existing therapies for inflammatory diseases also have toxic side effects. A challenge facing all research groups in this field has been the design of selective and specific immune system therapeutics that affect only the pathological activities without negatively affecting the protective activities of the immune system.

Our programs are designed to identify and validate novel molecules which specifically signal cell activation and cell death, or apoptosis, of T cells and B cells. Activation and apoptosis determine the quality, magnitude, and duration of immune responses. Activation pathways are initiated by the binding of antigen (foreign protein) to specific surface receptors on T cells or B cells. This sets off an intracellular cascade of signals, resulting in changes in gene expression and the production of proteins that drive the immune response or lead to antibody production and secretion in B cells. The apoptosis signals prevent self activation, overactivation or prolonged activation of the T and B cells, which can lead to auto-immune disease or organ rejection. We are identifying T cell and B cell-specific drug targets that are effective in modulating immune-mediated processes.

B CELL ACTIVATION. The goal of the B cell activation program is to prevent antibody secretion by activated B cells, an important mechanism in autoimmunity transplantation rejection. We have identified novel drug targets using our post-genomics combinatorial biology technology and have initiated high throughput screening. This program has been partnered with Novartis since August 1999.

T CELL ACTIVATION. The goal of our T cell program is to identify early steps in the process of T cell activation. T cells are responsible for cell-mediated inflammatory and humoral responses, both of which are important mechanisms of transplant rejection and autoimmune diseases. We have identified novel drug targets using our post-genomics combinatorial biology technology and have initiated high throughput screening. This program has been partnered with Novartis since May 1999.

RHEUMATOID ARTHRITIS AND INFLAMMATORY BOWEL DISEASE

We have programs directed at two different cellular pathways for these inflammatory diseases:

E-3 UBIQUITIN LIGASE. This program is focused on characterizing and developing specific inhibitors of protein-degrading enzymes, named E-3 ubiquitin ligases, in inflammation. The levels of many intracellular proteins that play a critical role in signaling pathways are regulated by this protein-degrading process. Many signaling proteins control cell function through active intermediates whose levels vary rapidly during different phases of a physiologic response. Disease processes can be treated by up-regulating or down-regulating these key signaling proteins as a way to enhance or dampen specific cellular responses. This principle has been successfully used in the design of a number of therapeutics for the treatment of inflammation. We also anticipate that, as the field of E-3 ubiquitin ligase biology evolves, inhibitors can be identified which will have clinical utility in metabolic diseases and possibly in neurodegenerative processes. We have screened over 100,000 small molecules against several members of the E-3 ubiquitin ligase family, and have identified several small molecule compounds which, based on preliminary data, appear to be potent and specific inhibitors.

SELECTED TNF PATHWAY TARGETS. This second program focuses on blocking the inflammatory signals of the Tumor Necrosis Factor, or TNF pathway, a pathway validated by existing antibody therapies as an important site for therapeutic intervention. We have identified and validated several novel members of this signaling pathway which are moving into both biochemical and cell based high throughput compound screens. Our preliminary results suggest that the targets we have identified in the TNF pathway regulate inflammatory responses in specific cell types, thus potentially making small molecule compounds directed at these targets more disease specific. In addition, these small molecules will be less likely to exhibit the side effects of chronic administration of anti-TNF antibodies or antibodies directed at the TNF receptor.

Additionally, our scientists have identified potential drug targets in the TNF pathway that protect T cells from apoptotic signals, and have used those interactions to identify a protective protein termed Toso. When T cells are activated, Toso production is activated and in turn causes other intracellular proteins to block apoptotic signals. Thus Toso may protect activated T cells from apoptosis. We are investigating Toso inhibition as a method of selectively killing activated disease-causing T cells.

CANCER

Cancer is a group of diseases characterized by the uncontrolled growth and proliferation of cells. This growth invades vital organs and often results in death. The United States market for branded cancer drugs totaled approximately

$7.0 billion in 1999 and is projected to grow at an 11% annual growth rate. Cancer is the second leading cause of death in the United States, exceeded only by cardiovascular disease. In 1999, an estimated 1.2 million people were diagnosed with cancer, and more than 500,000 patients died of cancer in the United States. Although there have been improvements in cancer therapies over the last decade, there remains a significant medical need for the development of both more effective and less toxic drugs for these diseases.

We are currently pursuing three important pathways directed against tumor growth:

CELL CYCLE INHIBITION. This program is directed toward the cell cycle checkpoint pathway. The proliferation of normal cells is controlled by built-in safety mechanisms in the cell cycle, termed checkpoints, that ensure that only cells with normal genetic material can progress through the cell cycle and divide. Cells with genetic mutations are recognized and shunted into the apoptosis pathway to protect the organism from cancer and other genetic disorders. It is estimated that more than 50 percent of all human tumors contain cancer cells that have lost one or more crucial checkpoint genes. Cancer cells also can carry mutations in another group of normal cell genes that mimic extracellular proliferation signals, causing tumor cells to continue to divide even in the absence of normal cell growth signals. The net result of these genetic mutations is uncontrolled cell division and disease. We have collaborated with our partner Janssen Pharmaceutica since December 1998 to identify intracellular drug targets involved in cell cycle control. We have identified several novel drug targets in this program, one of which has been accepted by Janssen Pharmaceutica as validated and has entered small molecule screens.

E-3 UBIQUITIN LIGASE. Our second antitumor program is focused on the E-3 ubiquitin ligase pathway unique to malignancies. The goal of this program is to examine specific inhibitors of ubiquitin ligases implicated in regulating mitosis, or cell division, in a number of transformed cell lines and normal cells. We also have identified a preclinical candidate compound in this program.

ANGIOGENESIS. Our third antitumor program is directed toward the angiogenesis pathway. Angiogenesis is defined as the growth of new blood vessels. In diseased circumstances or in oxygen deficient conditions, angiogenesis is stimulated by the synthesis and release of specific pro-angiogenic factors. In contrast to normal angiogenesis, tumor angiogenesis is a continuous process. As a significant proportion of tumors are dependent on continued angiogenesis, inhibition of this process blocks tumor growth which often leads to complete tumor deterioration. Thus, we believe therapeutic intervention of tumor-promoted angiogenesis represents an important form of anti-tumor therapy. We have established

and initiated two screens in human capillary endothelial cells using our post-genomics combinatorial biology technology in order to identify targets in the angiogenesis pathway.

RESEARCH AND DEVELOPMENT EXPENSES

Our research and development expenses were $14.6 million in the six months ended June 30, 2000, $17.1 million in 1999, $8.3 million in 1998 and $4.6 million in 1997.

CORPORATE COLLABORATIONS

To fund a wide array of research and development programs, we have established and will continue to pursue corporate collaborations with pharmaceutical and biotechnology companies. We currently have collaborations on six of our nine research programs, including one with Janssen Pharmaceutica relating to oncology therapeutics and diagnostics, one with Pfizer relating to asthma and allergy therapeutics, three with Novartis relating to immunology, and one with Cell Genesys relating to angiogenesis. In addition, we have collaborated with Neurocrine in order to obtain rights to small chemical compounds.

As of June 30, 2000, we had received a total of $29.1 million from our collaborators. Included in this amount is $10.0 million from participation in our preferred equity financing and $19.1 million for technology access and research funding, of which $3.3 million has been deferred at June 30, 2000. In addition, we have a number of scientific collaborations with academic institutions and biotechnology companies under which we have in-licensed technology. We intend to pursue further collaborations as appropriate.

In most of our collaborations, inventions are intended to be owned by the employer of the inventor or inventors thereof in accordance with United States patent law, subject to licenses or assignments granted in the agreements.

JANSSEN PHARMACEUTICA

Effective December 1998, we entered into a three-year research collaboration, ending December 2001, with Janssen Pharmaceutica, a Johnson &

Johnson company, to identify, discover, and validate novel drug targets that regulate cell cycle, and, specifically, the identification of drug targets and the active peptides that bind to them that can restore a mutated cell's ability to stop uncontrolled cell division. Under the agreement, we will provide certain assays and associated technology to Janssen Pharmaceutica for the assessment of the alteration or normalization of the dysfunctional cell cycles of cancer cells for Janssen Pharmaceutica's internal research purposes. Subsequently, in an amendment to the collaboration in July 2000, Janssen Pharmeceutica expanded the collaboration whereby we will be performing compound screening and medicinal chemistry on validated targets accepted by Janssen Pharmeceutica.

Janssen Pharmaceutica has accepted the first target identified during the collaboration as fully validated. Rigel and Janssen Pharmaceutica each has commenced high throughput screening of its respective compound libraries.

Under the collaboration, Janssen Pharmaceutica has the exclusive right to utilize our technology and technology developed during the collaboration to discover, develop, identify, make, and commercialize certain products on a worldwide basis. These products are:

- diagnostic products which are either a component of a drug target and associated active peptide, identified by or on behalf of us or Janssen Pharmaceutica in an assay developed during the collaboration, or identified in a Janssen Pharmaceutica screening assay as a result of Janssen Pharmaceutica's internal research;

- products identified by or on behalf of Janssen Pharmaceutica as a result of Janssen Pharmaceutica's internal research;

- products identified by or on behalf of either us or Janssen Pharmaceutica in an assay which incorporates a drug target and associated active peptide delivered to Janssen Pharmaceutica by us; and

- products which contain a component of a drug target and associated active peptide, or the functional equivalent of a component.

Janssen Pharmaceutica also has a non-exclusive right to use our technology, and technology developed during the research collaboration, to the extent necessary to use the assays we transfer to Janssen Pharmaceutica for internal research. Janssen Pharmaceutica's rights are subject to its obligation to provide research funding for the collaboration, make milestone payments and technology access payments to us, and pay royalties to us on the sales of products, as described above.

We will have the non-exclusive right to use any technology developed by Janssen Pharmaceutica during the research collaboration, and any improvements to our technology developed by Janssen Pharmaceutica during its internal research, on a royalty-free and worldwide basis. However, during the first 18 months after the signing date of the agreement, we may not enter into a research collaboration with a third party to identify drug targets and the associated active peptides which cause alterations in the cell cycle of human tumor cells.

The research collaboration will terminate (three years after the effective date of the agreement) unless the agreement is terminated, or the research collaboration is extended for up to two additional one year periods at Janssen Pharmaceutica's option.

The Johnson & Johnson Development Corporation, the investment entity affiliated with Janssen Pharmaceutica, purchased 1,500,000 shares of our Series D preferred stock at a price per share of $2.00 in connection with our Series D financing and in February 2000, purchased 166,666 shares of our Series E preferred stock at a price per share of $6.00 in connection with our Series E financing.

PFIZER

Effective January 1999, we entered into a two-year research collaboration with Pfizer, ending January 31, 2001 and renewable at Pfizer's option for an additional year. We do not, however, expect that our collaboration with Pfizer will be renewed. The goal of the collaboration is to identify intracellular drug targets that control the production of IgE, a key mediator in allergic reactions and asthma in B cells. We will provide the following technology developed or identified during and pursuant to the research collaboration to Pfizer:

- drug targets;

- technology associated with identified drug targets;

- technology necessary for Pfizer's performance of its research collaboration obligations; and

- technology necessary for Pfizer's performance of its research collaboration obligations; and

- technology necessary for Pfizer's performance of high throughput screening, or HTS, on identified drug targets.

Pfizer will exclusively own drug targets for which it has initiated HTS. We will have no obligation to Pfizer with regard to any drug target Pfizer does not select for HTS. During the research collaboration, we may not conduct research within the scope of the research collaboration by ourselves or with any third party except in connection with the research collaboration with Pfizer.

We and Pfizer each have the non-exclusive right to use for research purposes the technology of the other which is disclosed or developed during the research collaboration, excluding our peptide libraries and proprietary cell lines. Under the collaboration, Pfizer also has the exclusive, worldwide right to develop and market diagnostic and therapeutic products for humans and animals which were identified by Pfizer in HTS and modulate the activity of a drug target identified in the research collaboration. Pfizer's rights to develop and market such products are subject to its obligation to provide research funding to us for a minimum of two years, as well as cash for equity, technology access payments, research milestones, and royalties on the sales of these products.

In addition to typical termination events, Pfizer may terminate this agreement if Dr. Donald Payan's association with us as our chief scientific officer or similar role ends and we and Pfizer cannot agree on a successor acceptable to Pfizer.

Pfizer purchased 1,000,000 shares of Series D preferred stock at a price per share of $2.00 in connection with our Series D financing.

NOVARTIS

In May 1999, we signed an agreement for the establishment of a broad collaboration with Novartis, whereby the two companies will work on five different five-year research projects to identify drug targets for products that can treat, prevent, or diagnose the effects of human disease. Two of the research projects will be conducted jointly by Novartis and us, and the other three research projects will be conducted at Novartis. The first research project, a joint research project, is focused on identifying small molecule drug targets that regulate T cells. The second research project, also a joint research project, relates to the identification and validation of small molecule drug targets that can mediate specific functions of B cells. The third research project, a project carried out at Novartis, is focused on identifying small molecule drug targets that regulate pulmonary inflammation. Novartis will select the remaining two projects by May 2001.

Once a drug target from any of the five research projects has been identified and validated, Novartis shall have the right to conduct compound screening on such drug target on an exclusive basis for two years thereafter. Novartis will have the option to extend this exclusive right for up to five additional one-year periods so long as Novartis pays us an annual fee for such right and satisfies certain diligence conditions. Upon the expiration or termination of this right, both we and Novartis shall have the non-exclusive right to use, and allow others to use, such drug target for compound screening.

Under the agreement, Novartis has the non-exclusive right to utilize our post-genomics combinatorial biology technology and two hybrid protein interaction technology for confirmational and similar uses relating to validated drug targets, including uses necessary for the further development, registration, and commercialization of products whose principal mechanism of action is based upon, derived or discovered from, or discovered with the use of, a drug target. Novartis also has the exclusive right to utilize other of our technology and technology developed during the collaboration, to make and commercialize these products. Novartis' rights are subject to its obligation to provide research funding for the joint research projects, to pay milestone payments and technology access payments to us, and to pay third party royalties associated with Novartis' use of certain of our technology.

Under the agreement, we will have the non-exclusive right to use any improvements to our post-genomics combinatorial biology technology and two hybrid protein interaction technology developed during a research project on a royalty-free and worldwide basis.

Novartis may terminate the joint research projects two years after the applicable commencement date, or three and one half years after the applicable commencement date if Novartis gives six months prior notice of its termination. In some circumstances, Novartis also may terminate either of the joint research projects after the expiration of 12 months after the applicable commencement date. Novartis may terminate the research projects to be conducted at Novartis at any time.

Novartis purchased 2,000,000 shares of our Series D preferred stock at a per share purchase price of $2.00 in connection with our Series D financing. Novartis agreed, in certain circumstances, to purchase up to $10.0 million of our stock at our option. In September 2000, we exercised this right to sell

$10.0 million of our common stock in a private placement transaction concurrent with this public offering at the price per share at which our common stock will be sold in this offering.

CELL GENESYS

In September 1999, we established a research collaboration and license agreement with Cell Genesys. The goal of the research collaboration is to use our post-genomics combinatorial biology technology to identify novel therapeutic peptide, protein, and gene products in the field of gene therapy. Cell Genesys also will be granted exclusive, royalty-free worldwide rights to make, use, and commercialize therapeutic peptide, protein and gene products in the field of gene therapy. Cell Genesys also will be granted the right to make and use the intracellular drug targets with which their gene therapy products bind for the sole purpose of the research and development of gene therapy products. Cell Genesys also has the option to obtain rights under some of our cell lines and associated technology to make and commercialize gene therapy products.

In exchange for our performance of the research and the license granted to Cell Genesys, we were granted a royalty-free, worldwide right to some Cell Genesys patents and technology pertaining to retroviral gene delivery technology for use in the field of our post-genomics combinatorial biology. Each company will pay to the other company third-party sublicensing fees and royalties associated with the grant of the licenses discussed above, and fund their own research.

NEUROCRINE BIOSCIENCES

In addition to our nine programs focusing on specific disease mechanisms, effective December 1997, we conducted a research collaboration with Neurocrine to discover novel molecular targets involved in glial cell activation.

Under the terms of the agreement, Neurocrine has the exclusive, royalty-free right to utilize our technology and technology developed during the research collaboration to develop, make and commercialize on a worldwide basis, products which incorporate or are discovered using a drug target involved in glial cell activation or a peptide identified or produced by us which binds to this type of drug target. We have the exclusive, royalty-free right to utilize Neurocrine technology and technology developed during the research collaboration to develop, make and commercialize on a worldwide basis, products which incorporate or are discovered using a drug target not involved in glial cell activation or a peptide identified or produced by Neurocrine which does not bind to this type of drug target. Each company will assign to the other company its rights in proprietary technology and technology developed during the research collaboration which is related to the other company's products described above.

INTELLECTUAL PROPERTY

We will be able to protect our technology from unauthorized use by third parties only to the extent that it is covered by valid and enforceable patents or are effectively maintained as trade secrets. Accordingly, patents or other proprietary rights are an essential element of our business. We have 57 pending patent applications and one issued patent in the United States as well as corresponding foreign patent applications. At least seven patent applications had been filed in the United States by or on behalf of universities which had granted us exclusive license rights to the technology. To date, no patents have issued to us but we have received notification from the United States Patent Office that it intends to allow claims in three of our patent applications. Our policy is to file patent applications to protect technology, inventions and improvements to inventions that are commercially important to the development of our business. We seek United States and international patent protection for a variety of technologies,

including: new screening methodologies and other research tools; target molecules that are associated with disease states identified in our screens; and lead compounds that can affect disease pathways. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel drugs. We seek protection, in part, through confidentiality and proprietary information agreements. We are a party to various other license agreements that give us rights to use technologies in our research and development.

M&E has notified us that it expects to receive patent protection in European countries for a process similar to certain aspects of our technologies. M&E has indicated a willingness to license their intellectual property to us but has not specified the terms for the license. We are currently reviewing their patent file and evaluating whether or not to seek a license. We are also aware that M&E has the option to seek patent protection in other parts of the world, including the U.S., for the technology of its European patent protection. If M&E were to receive such patent protection, it might conflict with or overlap with the patent rights we are pursuing. We currently do not, and do not plan to, operate in any country outside the United States.

COMPETITION

We face, and will continue to face, intense competition from pharmaceutical and biotechnology companies, as well as academic and research institutions and government agencies, both in the United States and abroad. Some of these competitors are pursuing the development of pharmaceuticals that target the same diseases and conditions as our research programs. Our major competitors include fully integrated pharmaceutical companies that have extensive drug discovery efforts and are developing novel small molecule pharmaceuticals. We face significant competition from organizations that are pursuing the same or similar technologies, including the discovery of targets that are useful in compound screening, as the technologies used by us in our drug discovery efforts. Our competitors or their collaborative partners may utilize discovery technologies and techniques or partner more rapidly or successfully than we or our collaborators are able to do.

Many of these companies and institutions, either alone or together with their collaborative partners, have substantially greater financial resources and larger research and development staffs than we do. In addition, many of these competitors, either alone or together with their collaborative partners, have significantly greater experience than we do in:

- identifying and validating targets;

- screening compounds against targets; and

- undertaking preclinical testing and clinical trials.

Accordingly, our competitors may succeed in obtaining patent protection, identifying or validating new targets or discovering new drug compounds before us.

Competition may also arise from:

- new or better methods of target identification or validation;

- other drug development technologies and methods of preventing or reducing the incidence of disease;

- new small molecules; or

- other classes of therapeutic agents.

Developments by others may render our product candidates or technologies obsolete or noncompetitive. We face and will continue to face intense competition from other companies for collaborative arrangements with pharmaceutical and biotechnology companies, for establishing

relationships with academic and research institutions and for licenses to additional technologies. These competitors, either alone or with their collaborative partners, may succeed in developing technologies or products that are more effective than ours.

Our ability to compete successfully will depend, in part, on our ability to:

- identify and validate targets;

- discover candidate drug compounds which interact with the targets we identify;

- attract and retain scientific and product development personnel;

- obtain patent or other proprietary protection for our new drug compounds and technologies; and

- enter commercialization agreements for our new drug compounds.

GOVERNMENT REGULATION

If our potential preclinical compounds become ready to enter clinical testing, our ongoing development activities will be subject to extensive regulation by numerous governmental authorities in the United States and other countries, including the FDA under the Federal Food, Drug and Cosmetic Act. The regulatory review and approval process is expensive and uncertain. Securing FDA approval requires the submission of extensive preclinical and clinical data and supporting information to the FDA for each indication to establish a product candidate's safety and efficacy. The approval process takes many years, requires the expenditure of substantial resources and may involve ongoing requirements for post-marketing studies. Before commencing clinical investigations in humans, we must submit to, and receive approval from, the FDA of an IND. Clinical trials are subject to oversight by institutional review boards and the FDA and:

- must be conducted in conformance with the FDA's IND regulations;

- must meet requirements for institutional review board oversight;

- must meet requirements for informed consent;

- must meet requirements for good clinical practices;

- are subject to continuing FDA oversight;

- may require large numbers of participants; and

- may be suspended by us, our strategic partners, or the FDA at any time if it is believed that the subjects participating in these trials are being exposed to unacceptable health risks or if the FDA finds deficiencies in the IND or the conduct of these trials.

Even if we are able to achieve success in our clinical testing, we, or our collaborative partners, must provide the FDA and foreign regulatory authorities with clinical data that demonstrates the safety and efficacy of our products in humans before they can be approved for commercial sale. None of the product candidates that we have internally developed has advanced to the stage of human testing designed to determine safety, known as Phase I clinical trials. We do not know when or if clinical trials will begin and, once begun, will not know whether any such clinical trials will be successful or if such trials will be completed on schedule or at all. We do not know whether any future clinical trials will demonstrate sufficient safety and efficacy necessary to obtain the requisite regulatory approvals or will result in marketable products. Our failure, or the failure of our strategic partners, to adequately demonstrate the safety and efficacy of our products under development will prevent receipt of FDA and similar foreign regulatory approval and, ultimately, commercialization of our products.

Any clinical trial may fail to produce results satisfactory to the FDA. Preclinical and clinical data can be interpreted in different ways, which could delay, limit or prevent regulatory approval. Negative or

inconclusive results or adverse medical events during a clinical trial could cause a clinical trial to be repeated or a program to be terminated. In addition, delays or rejections may be encountered based upon additional government regulation from future legislation or administrative action or changes in FDA policy or interpretation during the period of product development, clinical trials and FDA regulatory review. Failure to comply with applicable FDA or other applicable regulatory requirements may result in criminal prosecution, civil penalties, recall or seizure of products, total or partial suspension of production or injunction, as well as other regulatory action against our potential products, collaborative partners or us. Additionally, we have no experience in working with our partners in conducting and managing the clinical trials necessary to obtain regulatory approval.

Outside the United States, our ability to market a product is contingent upon receiving a marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical trials, marketing authorization, pricing and reimbursement vary widely from country to country. At present, foreign marketing authorizations are applied for at a national level, although within the European Union, or EU, registration procedures are available to companies wishing to market a product in more than one EU member state. If the regulatory authority is satisfied that adequate evidence of safety, quality and efficacy has been presented, a marketing authorization will be granted. This foreign regulatory approval process involves all of the risks associated with FDA clearance.

Because we moved to a new facility in March 1999 designed to comply with all applicable federal, state and local environmental and hazardous waste regulations, we expect no additional substantial expenditures for this purpose. The facility was also designed to comply with current earthquake design criteria.

EMPLOYEES

As of August 31, 2000, we employed 102 persons, of whom 29 hold PhD or MD degrees and seven hold other advanced degrees. Approximately 85 employees are engaged in research and development, and 17 support administration, finance, management information systems, facilities and human resources. None of our employees is represented by a collective bargaining agreement, nor have we experienced work stoppages. We believe that our relations with our employees are good.

FACILITIES

Our facilities consist of approximately 61,000 square feet of research and office space located at 240 East Grand Avenue, South San Francisco, California that is leased to us until 2016. We have options to renew this lease for two additional periods of five years each. We believe our facility will meet our space requirements for research and development and administration functions through the year 2001.

LEGAL PROCEEDINGS

We are not a party to any pending material litigation.

SCIENTIFIC ADVISORY BOARD

We utilize scientists and physicians to advise us on scientific and medical matters as part of our Scientific Advisory Board including, experts in human genetics, mouse genetics, molecular biology, biochemistry, cell biology, chemistry, infectious diseases, immunology and structural biology. Generally, each of our scientific and medical advisors and consultants receives an option to purchase our common stock and an honorarium for time spent assisting us. The following is a list of our Scientific Advisory Board members:

GARRY P. NOLAN, PHD, our co-founder and Chairman of the Scientific Advisory Board, is Associate Professor in the Department of Molecular Pharmacology and Department of Microbiology and Immunology at Stanford University Medical Center.

ROBIN G. COOPER, DSC, PHD is a former Research Advisor at Eli Lilly and Co., and presently President of Cooper Consulting Inc.

CHARLES S. CRAIK, PHD is Professor of Pharmaceutical Chemistry and Pharmacology, Biochemistry and Biophysics, and Director of the Chemistry and Chemical Biology Graduate Group at the University of California San Francisco.

DANIEL R. LITTMAN, MD PHD is the Coordinator of the Molecular Pathogenesis Program, Skirball Institute of Biomolecular Medicine and Professor of Microbiology and Pathology at the New York University School of Medicine and Investigator, Howard Hughes Medical Institute.

RICHARD M. LOCKSLEY, MD is Professor, Departments of Medicine and Microbiology/Immunology, Chief of the Division of Infectious Diseases and Investigator, Howard Hughes Medical Institute, at the University of California San Francisco.

RICHARD SCHELLER, PHD is Professor of Molecular and Cellular Physiology and Investigator, Howard Hughes Medical Institute at Stanford University.

KEVAN M. SHOKAT, PHD is Associate Professor of Cellular and Molecular Pharmacology at the University of California San Francisco and Associate Professor, Department of Chemistry at University of California Berkeley.

JOHN B. TAYLOR, DSC, PHD is the former Sr. Vice President for WW Pharmaceutical Discovery Operations with Rhone Poulenc Rorer (Aventis) and presently a Pharmaceutical R&D Consultant.

RICHARD ULEVITCH, PHD is Chairman of the Department of Immunology at the Scripps Research Institute.

MATTHIAS WABL, PHD is Professor of Microbiology and Immunology in the Department of Microbiology and Immunology at the University of California San Francisco.

CLINICAL ADVISORY BOARD

In addition to our Scientific Advisory Board, we utilize a number of scientists and physicians to advise us on the scientific and medical matters associated with clinical trials. This group is known as our Clinical Advisory Board. The following is a list of our Clinical Advisory Board members:

THOMAS A. RAFFIN, MD, our co-founder and Chairman of our Clinical Advisory Board, is the Colleen and Robert Haas Professor of Medicine and Biomedical Ethics, Chief of the Division of Pulmonary and Critical Care Medicine and Co-Director of the Center for Biomedical Ethics at Stanford University Medical Center.

DENNIS A. CARSON, MD is Professor of Medicine in the Department of Medicine at the University of California San Diego and Director of the Sam and Rose Stein Institute on Aging.

ALAN R. LEFF, MD is Professor of Medicine, Neurobiology, Pharmacology and Physiology, Pediatrics, Anesthesia and Critical Care, Clinical Pharmacology and Cell Physiology, and Senior Director for Research and Development for the Biological Science Division at the University of Chicago, Chicago, Illinois.

ROBERT S. MUNFORD, MD is Professor of Internal Medicine and Microbiology at the University of Texas Southwestern Medicine Center in Dallas, Texas.

GLENN D. ROSEN, MD is Associate Professor of Medicine in the Division of Pulmonary and Critical Care Medicine at Stanford University Medical Center.

EXECUTIVE OFFICERS AND DIRECTORS

Set forth below is the name, age, position and a brief account of the business experience of each of our executive officers and directors.

<TABLE>
<CAPTION>

NAME	AGE	POSITION
<S>	<C>	<C>
James M. Gower	52	President, Chief Executive Officer and Director
Donald G. Payan, MD	52	Executive Vice President and Chief Scientific Officer and Director
Brian C. Cunningham	56	Senior Vice President, Chief Operating Officer, Chief Financial Officer and Secretary
James H. Welch	42	Vice President, Finance and Administration and Assistant Secretary
Raul R. Rodriguez	39	Vice President, Business Development
Jean Deleage, PhD(1)	59	Director
Alan D. Frazier(2)	48	Director
Walter H. Moos, PhD(1)(2)	46	Director
Stephen A. Sherwin, MD(1)	51	Director
Thomas S. Volpe	49	Director

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(1) Member of the audit committee.

(2) Member of the compensation committee.

JAMES M. GOWER joined us as our President, Chief Executive Officer and as a member of our board of directors in January 1997. From 1992 to March 1996, Mr. Gower was President and Chief Executive Officer of Tularik, Inc., a biotechnology company developing small-molecule drugs regulating gene expression. Prior to Tularik, Mr. Gower spent ten years at Genentech, Inc., a biopharmaceutical company, where he most recently served as Senior Vice President. During his ten years at Genentech, Mr. Gower was responsible for business development and sales and marketing functions. In addition, he established and managed Genentech's foreign operations in Canada and Japan and served as President of Genentech Development Corporation. Mr. Gower serves on the board of directors of Cell Genesys, Inc. He holds a BS and an MBA in operations research from the University of Tennessee.

DONALD G. PAYAN, MD is our co-founder, has been a member of our board of directors since July 1996 and has served as our Executive Vice President and Chief Scientific Officer since January 1997. From January 1997 to July 1998, he also served as our Chief Operating Officer. From July 1996 to January 1997, Dr. Payan served as our President and Chief Executive Officer. From December 1995 to May 1996, Dr. Payan was Vice President of AxyS Pharmaceuticals, Inc., a biopharmaceutical company. From September 1993 to December 1995, Dr. Payan was the founder and Executive Vice President and Chief Scientific Officer of Khepri Pharmaceuticals, Inc., which merged with AxyS Pharmaceuticals. Dr. Payan continues his association with the University of California, San Francisco, which began in 1982, where he is currently an Adjunct Professor of Medicine and Surgery. Dr. Payan holds a BS and an MD from Stanford University.

BRIAN C. CUNNINGHAM has been our Secretary since July 1996. In July 1998, he joined us as Senior Vice President and Chief Operating Officer, and in February 1999, he also became our Chief Financial Officer. From January 1989 to September 1998, Mr. Cunningham was a partner in the law firm Cooley Godward LLP where he was head of the Life Sciences Group and the Health Care Group and is currently Of Counsel. From May 1982 to December 1989, he served as Vice President, Secretary and General Counsel

of Genentech Inc. Mr. Cunningham holds a BS in engineering science and a JD from Washington University.

JAMES H. WELCH joined us as our Vice President, Finance and Administration and Assistant Secretary in May 1999. From June 1998 to May 1999, he served as an independent consultant at various companies. From February 1997 to June 1998, Mr. Welch served as Chief Financial Officer of Biocircuits Corporation, a manufacturer of medical diagnostic equipment, and from June 1992 to February 1997, he served as Corporate Controller of Biocircuits. Previously, Mr. Welch held various positions at NeXT Computer, Inc., most recently as Division Controller. Mr. Welch holds a BA in business administration from Whitworth College and an MBA from Washington State University.

RAUL R. RODRIGUEZ joined us as our Vice President, Business Development in

April 2000. From 1997 to March 2000, he served as Senior Vice President, Business Development and Operations for Ontogeny, Inc., a biotechnology company. From 1994 to 1997, he served as the Executive Director, Business Development and Market Planning for Scios, Inc., a pharmaceutical company. Mr. Rodriguez holds an AB in history and science from Harvard College, an MPH from the University of Illinois and an MBA from Stanford University.

JEAN DELEAGE, PHD joined us as a director in January 1997. Dr. Deleage is a founder and managing director of Alta Partners, a venture capital firm investing in information technologies and life sciences companies. From 1979 to 1996, Dr. Deleage was a managing partner of Burr, Egan, Deleage & Co., a venture capital firm. Dr. Deleage was the founder of Sofinnova, a venture capital organization in France, and Sofinnova, Inc., the U.S. subsidiary of Sofinnova. Dr. Deleage currently serves on the board of directors of Flamel Technologies S.A., Aclara Biosciences, Inc. and Telik, Inc. Dr. Deleage received a Baccalaureate in France, a Masters Degree in electrical engineering from the Ecole Superieure d'Electricite and a PhD in Economics from the Sorbonne.

ALAN D. FRAZIER joined us as a director in October 1997. In 1991, Mr. Frazier founded Frazier & Company, a venture capital firm, and has served as the managing principal since its inception. From 1983 to 1991, Mr. Frazier served as Executive Vice President, Chief Financial Officer and Treasurer of Immunex Corporation, a biopharmaceutical company. From 1980 to 1983, Mr. Frazier was a principal in the Audit Department of Arthur Young & Company (now Ernst & Young). He also serves on the board of trustees of the Fred Hutchinson Cancer Research Center, the Technology Alliance of Washington, Voyager Capital's Advisory Board and the Washington Venture Capital Association. Mr. Frazier holds a BA in economics from the University of Washington.

WALTER H. MOOS, PHD joined us as a director in March 1997. Since 1997, Dr. Moos has served as the Chairman and Chief Executive Officer of MitoKor, a biotechnology company. From 1991 to 1997, he served as Corporate Vice President and Vice President, Research and Development in the Technologies Division of Chiron Corporation, a biotechnology company. From 1982 to 1991, Dr. Moos held several positions at the Parke-Davis Pharmaceutical Research Division of the Warner-Lambert Company, last holding the position of Vice President, Neuroscience and Biological Chemistry. He has been an Adjunct Professor at the University of California, San Francisco, since 1992. Dr. Moos holds an AB from Harvard University and a PhD in chemistry from the University of California, Berkeley.

STEPHEN A. SHERWIN, MD joined us as a director in March 2000. Since March 1990, he has served as President, Chief Executive Officer and director of Cell Genesys, Inc. and as Chairman of the Board of Cell Genesys since March 1994. From 1983 to 1990, Dr. Sherwin held various positions at Genentech Inc., most recently as Vice President, Clinical Research. He received his MD from Harvard Medical School and his BA from Yale University. Dr. Sherwin also currently serves as a director of Abgenix, Inc. and Neurocrine Biosciences, Inc.

THOMAS S. VOLPE joined as a director in August 2000. Since December 1999, he has served as the Chairman of Prudential Volpe Technology Group. Mr. Volpe also serves on the board of directors of

Linear Technology Corporation. From 1986 to 1999, Mr. Volpe was President, CEO and founder of Volpe Brown Whelan & Company, a risk capital and investment banking firm focused on rapidly growing entrepreneurial companies. Prior to forming Volpe Brown Whelan & Company, he was President, CEO and a member of the Board of Directors and Management Committee of Hambrecht & Quist Incorporated. Before joining Hambrecht & Quist, Mr. Volpe was Head of the Science and Technology Group of Blyth Eastman PaineWebber. Mr. Volpe holds an AB in Economics from Harvard University, a MSc in economics from the London School of Economics and an MBA from the Harvard Business School.

Our executive officers are appointed by our board of directors and serve until their successors are elected or appointed. There are no family relationships among any of our directors or executive officers. No director has a contractual right to serve as a member of our board of directors.

BOARD COMMITTEES

AUDIT COMMITTEE

Our audit committee, consisting of Drs. Deleage, Sherwin and Moos, reviews our internal accounting procedures and the services provided by our independent auditors.

COMPENSATION COMMITTEE

Our compensation committee, consisting of Mr. Frazier and Dr. Moos, reviews and recommends to our board of directors the compensation and benefits of all our officers and establishes and reviews general policies relating to compensation and benefits of our employees.

DIRECTOR COMPENSATION

We do not provide cash compensation to members of our board of directors for serving on our board of directors or for attendance at committee meetings. Members of our board of directors are reimbursed for some expenses in connection with attendance at board and committee meetings. In consideration for services as a non-employee director, on November 12, 1998, we granted an option to purchase 20,000 shares of common stock to Dr. Moos at an exercise price of $.20 per share. The $.20 per share exercise price for these options was equal to the fair market value of the common stock on the date of grant as determined by our board of directors. These options vest in a series of 36 equal monthly installments beginning on the grant date of the option. On March 8, 2000 and August 2, 2000, we granted options to purchase 20,000 and 6,341 shares of common stock to Dr. Sherwin at exercise prices of $11.00 and $4.50 per share, respectively. These options vest in a series of 24 equal monthly installments beginning on the grant date of the option.

COMPENSATION COMMITTEE INTERLOCKS AND INSIDER PARTICIPATION

Our compensation committee currently consists of Mr. Frazier and Dr. Moos. Mr. Gower served on our compensation committee from February 1998 to January 2000. No current member of the compensation committee has been an officer or employee of ours at any time. None of our executive officers serves as a member of the board of directors or compensation committee of any other company that has one or more executive officers serving as a member of our board of directors or compensation committee. Prior to the formation of a compensation committee in February 1998, the board of directors as a whole made decisions relating to compensation of our executive officers.

EXECUTIVE COMPENSATION

The following table sets forth information concerning the compensation that we paid during 1999 to our Chief Executive Officer and each of the four other most highly compensated executive officers that earned more than $100,000 during 1999. All option grants were made under our 1997 Stock Option Plan.

<TABLE>
<CAPTION>

	ANNUAL COMPENSATION		LONG TERM COMPENSATION
NAME AND PRINCIPAL POSITION	SALARY	BONUS	SECURITIES UNDERLYING OPTIONS/SARS
<S>	<C>	<C>	<C>
James M. Gower..... President, Chief Executive Officer and Director	$255,000	--	450,000
Donald G. Payan..... Executive Vice President and Chief Scientific Officer and Director	235,417	--	150,000
Brian C. Cunningham(1)..... Senior Vice President, Chief Operating Officer, Chief Financial Officer and Secretary	250,000	--	--
James H. Welch(2)..... Vice President, Finance and Administration and Assistant Secretary	100,000	$25,000	150,000
Donald W. Perryman(3)..... Former Vice President, Business Development	140,000	--	--

</TABLE>

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(1) In January 2000, we granted Mr. Cunningham an option to purchase 200,000 shares of common stock at an exercise price of $4.50 per share, which was equal to the fair market value of the common stock on the date of grant as determined by the board of directors. These options vest monthly over a four-year period from the date of grant.

(2) Mr. Welch joined Rigel in May 1999. His annualized 1999 salary was $150,000. In January 2000, we granted Mr. Welch an option to purchase 50,000 shares of common stock at an exercise price of $4.50 share, which was equal to the fair market value of the common stock on the date of grant as determined by the board of directors. These options vest monthly over a four-year period.

(3) Mr. Perryman resigned as Vice President, Business Development, effective January 15, 2000.

The following table sets forth summary information regarding the option grants made to our Chief Executive Officer and each of our four other most highly paid executive officers during 1999. Options granted to purchase shares of our common stock under our 1997 Stock Option Plan generally vest over a four-year or five-year period. The exercise price per share is equal to the fair market value of our common stock on the date of grant as determined by our board of directors. In determining the fair market value of our common stock on the

date of grant our board of directors considered many factors, including:

- the fact that option grants involved illiquid securities in a nonpublic company;

- prices of preferred stock issued by Rigel to outside investors in arm's-length transactions, and the rights, preferences and privileges of the preferred stock over the common stock;

- Rigel's performance and operating results at the time of grant;

- the status of Rigel's research and development efforts;

- Rigel's stage of development and business strategy; and

- the likelihood of achieving a liquidity event for the shares of common stock underlying these options, such as an initial public offering or a sale of Rigel.

The potential realizable value is calculated based on the ten-year term of the option at the time of grant. Stock price appreciation of 5% and 10% is assumed pursuant to rules promulgated by the Securities and Exchange Commission and does not represent our prediction of our stock price performance. The potential realizable values at 5% and 10% appreciation are calculated by:

- multiplying the number of shares of common stock under the option by the assumed initial public offering price of $9.00 per share;

- assuming that the aggregate stock value derived from that calculation compounds at the annual 5% or 10% rate shown in the table until the expiration of the options; and

- subtracting from that result the aggregate option exercise price.

Percentages shown under "Percentage of Total Options Granted to Employees in 1999" are based on an aggregate of 2,449,000 options granted to employees under our 1997 Stock Option Plan during 1999.

OPTION GRANTS IN LAST FISCAL YEAR ENDED DECEMBER 31, 1999

<TABLE>
<CAPTION>

	INDIVIDUAL GRANTS				POTENTIAL REALIZABLE VALUE AT ASSUMED ANNUAL RATES OF APPRECIATION OF STOCK PRICE FOR OPTION TERM	
NAME	NUMBER OF SECURITIES UNDERLYING OPTIONS GRANTED	% OF TOTAL OPTIONS GRANTED TO EMPLOYEES IN 1999	EXERCISE PRICE $/SH	EXPIRATION DATE	5%	10%
<S>	<C>	<C>	<C>	<C>	<C>	<C>
James M. Gower.....	450,000	18.4%	$.20	2/11/09	6,507,023	10,414,657
Donald G. Payan.....	150,000	6.1%	.20	2/11/09	2,169,008	3,471,552
Brian C. Cunningham.....	--	--%	--	--	--	-
James H. Welch.....	150,000	6.1%	.20	5/11/09	2,169,008	3,471,552
Donald W. Perryman.....	--	--%	--	--	--	-

</TABLE>

The following table sets forth summary information regarding the number and value of options held as of December 31, 1999 for our Chief Executive Officer and each of our four most highly compensated executive officers. In the eight-month period ended August 31, 2000, Mr. Cunningham, our Chief Operating Officer and Chief Financial Officer acquired 100,000 shares and Mr. Welch, our Vice President, Finance and Administration, acquired 37,500 shares upon the exercise of options. Neither our Chief Executive Officer nor any of our four most highly compensated executive officers acquired any shares upon exercise of options in 1999. Amounts shown in the value of unexercised in-the-money options at December 31, 1999 column are based on an initial public offering price of $9.00 per share without taking into account any taxes that may be payable in connection with the transaction, multiplied by the number of shares underlying the option, less the aggregate exercise price payable for these shares.

AGGREGATED OPTION EXERCISES IN LAST FISCAL YEAR AND FISCAL YEAR-END OPTION VALUES

<TABLE>
<CAPTION>

		NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS AT DECEMBER 31, 1999	VALUE OF UNEXERCISED IN-THE-MONEY OPTIONS AT DECEMBER 31, 1999

NAME	VESTED	UNVESTED	VESTED	UNVESTED
<S>	<C>	<C>	<C>	<C>
James M. Gower	75,000	375,000	$ 660,000	$ 3,300,000
Donald G. Payan	25,000	125,000	220,000	1,100,000
Brian C. Cunningham	141,666	358,334	1,253,744	3,171,256
James H. Welch	--	150,000	--	1,320,000
Donald W. Perryman	58,333	41,667	519,164	370,836

</TABLE>

EMPLOYEE BENEFIT PLANS

2000 EQUITY INCENTIVE PLAN

Our board of directors adopted our 2000 Equity Incentive Plan on January 27, 2000, which was subsequently approved by our stockholders on March 15, 2000. The 2000 Equity Incentive Plan is an amendment and restatement of our 1997 Stock Option Plan.

SHARE RESERVE

We have reserved a total of 9,525,000 shares of our common stock for issuance under the incentive plan. If the recipient of a stock award does not purchase the shares subject to such stock award before the stock award expires or otherwise terminates, the shares that are not purchased will again become available for issuance under the incentive plan.

ADMINISTRATION

The board administers the incentive plan unless it delegates administration to a committee. The board has the authority to construe, interpret and amend the incentive plan as well as to determine:

- who will receive awards under the incentive plan;
- the dates on which such awards will be granted;
- the number of shares subject to the awards;
- the vesting and/or exercisability of the awards;
- the exercise price of the awards;
- the type of consideration that may be used to satisfy the exercise price; and
- the other terms of the awards.

ELIGIBILITY

The board may grant incentive stock options that qualify under Section 422 of the Internal Revenue Code to our employees and to the employees of our affiliates. The board also may grant nonstatutory stock options, stock bonuses and restricted stock purchase awards to our employees, directors and consultants as well as to the employees, directors and consultants of our affiliates.

Our incentive plan includes the following features:

- a stock option is a contractual right to purchase a specified number of our shares at a specified price (exercise price) during a specified period of time.
- an incentive stock option is a stock option that meets the requirements of Section 422 of the Internal Revenue Code. The holder of such an option will not be required to pay tax on either the date of grant or the date of exercise. If two holding period tests are met-more than two years between grant date and sale date and more than one year between exercise date and sale date-the optionholder will be taxed on the profit received on the subsequent disposition of the option stock as long-term capital gain. If the holding periods are not met, there has been a disqualifying disposition, and the difference between the exercise price and the fair market value of the shares on the exercise date will be taxed at ordinary income rates. The difference between the fair market value on date of exercise and the exercise price is an item of adjustment for purposes of the alternative minimum tax unless there is a disqualifying disposition in the year of exercise.
- a nonstatutory stock option is a stock option that does not meet the Internal Revenue Code criteria for qualifying as an incentive stock option. Upon exercise of a nonstatutory option, the option

holder will be required to pay state and federal income tax and, if

applicable, federal employment taxes on the difference between the exercise price and the fair market value on the exercise date.

- a restricted stock purchase award is an offer to purchase shares at a price that is at or near the fair market value of the shares. A stock bonus, on the other hand, is a grant of our shares at no cost to the recipient in consideration for past services rendered. Such awards generally are subject to a vesting schedule pursuant to which we may reacquire the shares subject to the award at the original purchase price (which is zero in the case of a stock bonus) if the recipient's service to us and our affiliates terminates before the shares vest.

The board may not grant an incentive stock option to any person who, at the time of the grant, owns or is deemed to own stock possessing more than 10% of our total combined voting power or the total combined voting power of an affiliate of ours, unless the exercise price is at least 110% of the fair market value of the stock on the grant date and the option term is no more than five years.

LIMITS ON OPTION GRANTS

There are limits on the number of shares that the board may grant under an option.

- section 162(m) of the Internal Revenue Code denies a deduction to publicly held corporations for compensation paid to the corporation's chief executive officer and its four highest compensated officers in a taxable year to the extent that the compensation for each such officer exceeds $1,000,000. When we become subject to Section 162(m), in order to prevent options granted under the incentive plan from being included in such compensation, the incentive plan provides that the board may not grant options under the incentive plan to any employee covering an aggregate of more than 1,500,000 shares in any calendar year.

- an employee may not receive incentive stock options that exceed the $100,000 per year limitation set forth in Section 422(d) of the Internal Revenue Code. In calculating the $100,000 per year limitation, we consider the aggregate number of shares under all incentive stock options granted to that employee that will become exercisable for the first time during a calendar year. For this purpose, we include incentive stock options granted under the incentive plan as well as under any other stock plans that we and our affiliates maintain. We then determine the aggregate fair market value of shares subject to all such incentive stock options as of the grant date of the options. Taking the options into account in the order in which they were granted, we treat only the options covering the first $100,000 worth of stock as incentive stock options. We treat any options covering stock in excess of $100,000 as nonstatutory stock options.

OPTION TERMS

The board may grant incentive stock options with an exercise price of 100% or more of the fair market value of a share of our common stock on the grant date. It may grant nonstatutory stock options with an exercise price as low as 85% of the fair market value of a share on the grant date.

THE MAXIMUM OPTION TERM IS TEN YEARS

The maximum term of options granted under our equity incentive plan is ten years. The board may provide for exercise periods of any length following an optionholder's termination of service in individual option grants. However, generally options will provide that they terminate three months after the optionholder's service to us and our affiliates terminates. If such termination is due to the optionholder's disability, the exercise period generally is extended 12 months unless the term of the option expires prior to that date in accordance with the terms of the individual's option agreement. If such termination is due to the optionholder's death, or if the optionholder dies within three months after his or her service terminates, the exercise period generally is extended to 18 months following the optionholder's death

unless the term of the option expires prior to that date in accordance with the terms of the individual's option agreement.

The board may provide for the transferability of nonstatutory stock options but not incentive stock options. However, the optionholder may designate a beneficiary to exercise either type of option following the optionholder's death. If the optionholder does not designate a beneficiary, the optionholder's option rights will pass to his or her heirs will or the laws of descent and distribution.

TERMS OF OTHER STOCK AWARDS

The board determines the purchase price of other stock awards, which may not be less than 85% of the fair market value of our common stock on the grant date.

However, the board may award stock bonuses in consideration of past services without a cash purchase price. Shares that we sell or award under the incentive plan may, but need not be, restricted and subject to a repurchase option in our favor in accordance with a vesting schedule that the board determines. The board, however, may accelerate the vesting of such awards.

OTHER PROVISIONS

Transactions not involving our receipt of consideration, such as a merger, consolidation, reorganization, stock dividend, or stock split, may change the class and number of shares subject to the incentive plan and to outstanding awards. In that event, the board will appropriately adjust the incentive plan as to the class and the maximum number of shares subject to the incentive plan and to the Section 162(m) limit. It also will adjust outstanding awards as to the class, number of shares and price per share applicable to such awards.

If we dissolve or liquidate, then-outstanding stock awards will terminate immediately prior to such event. However, we treat outstanding stock awards differently in the following situations:

- a sale, lease or other disposition of all or substantially all of our assets or securities;

- a merger or consolidation in which we are not the surviving corporation; or

- a reverse merger in which we are the surviving corporation but the shares of our common stock outstanding immediately before the merger are converted by virtue of the merger into other property, such as securities or cash.

In these situations, the surviving corporation may either assume all outstanding awards under the incentive plan or substitute other awards for the outstanding awards. If the surviving corporation does not assume or substitute, then, for award holders who are then providing services to us or our affiliates, the vesting and exercisability of the awards will accelerate and the awards will terminate immediately prior to the occurrence of the event described above. The vesting and exercisability of awards held by award holders who are no longer providing services to us or one of our affiliates will not accelerate. However, those awards will also terminate immediately prior to the occurrence of the event described above.

STOCK AWARDS GRANTED

As of August 31, 2000, 2,063,909 shares were issued upon the exercise of options under our equity incentive plan, 2,500 shares of which have been repurchased; 100,000 shares were issued upon stock bonuses; options to purchase 5,622,370 shares were outstanding; and 1,738,721 shares remained available for grant.

PLAN TERMINATION

The incentive plan will terminate in 2010 unless the board terminates it sooner.

2000 NON-EMPLOYEE DIRECTORS' STOCK OPTION PLAN

Our board of directors adopted the 2000 Non-Employee Directors' Stock Option Plan on August 18, 2000, which was subsequently approved by our stockholders on September 11, 2000. The directors' plan will become effective on the effective date of this initial public offering. The directors' plan provides for the automatic grant to our non-employee directors of options to purchase shares of our common stock.

SHARE RESERVE

We have reserved a total of 300,000 shares of our common stock for issuance under the directors' plan.

If an optionholder does not purchase the shares subject to such option before the option expires or otherwise terminates, the shares that are not purchased again become available for issuance under the directors' plan.

ADMINISTRATION

The board administers the directors' plan. The board has the authority to construe, interpret and amend the directors' plan, but the directors' plan specifies the essential terms of the options, including:

- who will receive options under the directors' plan;

- the dates on which such options will be granted;

- the number of shares subject to the options;

- the vesting schedule applicable to the options;

- the exercise price of the options; and

- the type of consideration that may be used to satisfy the exercise price.

ELIGIBILITY

Each non-employee director who is serving on the effective date of this offering will automatically be granted an option to purchase 20,000 shares of common stock. Each person who is elected or appointed to be a non-employee director for the first time after the effective date of this offering will be granted an option to purchase 20,000 shares of common stock upon such election or appointment. In addition, each non-employee director who continues to serve as a non-employee director automatically will be granted an option to purchase 5,000 shares of common stock on the day following each annual meeting of our stockholders commencing in 2001. The number of shares subject to the grants to be made following each annual meeting will be pro-rated for any non-employee director who has not continuously served as a director for the entire 12-month period prior to the date of grant. The options will vest over two years in equal monthly installments provided that the non-employee director continues to provide services to us or one of our affiliates.

OPTION TERMS

Options granted under the directors' plan will have an exercise price equal to 100% of the fair market value of the common stock on the grant date and a term of two years. As long as a non-employee director continues to serve with us or with an affiliate of ours, whether in the capacity of a director, an employee or a consultant, the non-employee's option will continue. Options will terminate three months after the optionholder's service terminates. However, if such termination is due to the optionholder's disability, the exercise period will be extended to 12 months unless the term of the option expires prior to that date in accordance with the terms of the individual's option agreement. If such termination is due to the optionholder's death or if the optionholder dies within three months after his or her service terminates, the

exercise period will be extended to 18 months following death unless the term of the option expires prior to that date in accordance with the terms of the individual's option agreement.

Optionholders may transfer options granted under the directors' plan by gift to immediate family or, under certain circumstances, to a trust for estate-planning purposes. Optionholders also may designate a beneficiary to exercise their options following the optionholder's death. Otherwise, option exercise rights will pass by the optionholder's will or by the laws of descent and distribution.

OTHER PROVISIONS

Transactions not involving our receipt of consideration, such as a merger, consolidation, reorganization, stock dividend or stock split, may change the class and number of shares subject to the directors' plan and to outstanding options. In that event, the board will appropriately adjust the directors' plan as to the class and the maximum number of shares subject to the directors' plan. It also will adjust outstanding options as to the class, number of shares and price per share applicable to such options.

If we dissolve or liquidate, then outstanding options will terminate immediately prior to such event. However, we treat outstanding options differently in the following situations:

- a sale, lease or other disposition of all or substantially all of our assets or securities;

- a merger or consolidation in which we are not the surviving corporation; or

- a reverse merger in which we are the surviving corporation but the shares of our common stock outstanding immediately before the merger are converted by virtue of the merger into other property, such as securities or cash.

In these situations, the surviving corporation will either assume the options outstanding under the directors' plan or substitute other options for the outstanding options. If the surviving corporation does not assume or substitute all outstanding options under the directors' plan, then for optionholders who are then providing services to us or one of our affiliates, the vesting and exercisability of the options will accelerate and the options will terminate if they are not exercised prior to the event described above. The vesting and exercisablity of options held by optionholders who are no longer providing services to us or one of our affiliates will not accelerate. However, these options also will terminate immediately prior to the occurrence of the

event described above.

OPTIONS ISSUED

We have not issued any options under the directors' plan.

PLAN TERMINATION

The directors' plan will terminate in 2010 unless the board terminates it sooner.

2000 EMPLOYEE STOCK PURCHASE PLAN

Our board of directors adopted the 2000 Employee Stock Purchase Plan on August 18, 2000, which was subsequently approved by our stockholders on September 11, 2000. The employee stock purchase plan will become effective on the effective date of this initial public offering.

SHARE RESERVE

We have authorized the issuance of 400,000 shares of our common stock pursuant to purchase rights granted to eligible employees under the purchase plan. On each anniversary of the effective date of this offering, starting with the anniversary of this offering in 2001, the share reserve will automatically be increased by a number of shares equal to the lesser of:

- 1% of our then outstanding shares of common stock;

- 400,000 shares; or

- a number determined by our board of directors.

ELIGIBILITY

The purchase plan is intended to qualify as an employee stock purchase plan within the meaning of Section 423 of the Internal Revenue Code. The purchase plan provides a means by which eligible employees may purchase our common stock through payroll deductions. We implement the purchase plan by offerings of purchase rights to eligible employees. Generally, all of our full-time employees and full-time employees of our affiliates incorporated in the United States may participate in offerings under the purchase plan. However, no employee may participate in the purchase plan if, immediately after we grant the employee a purchase right, the employee has voting power over 5% or more of our outstanding capital stock. As of the date hereof, no shares of common stock had been purchased under the purchase plan.

ADMINISTRATION

Under the purchase plan, the board may specify offerings of up to 27 months. Unless the board otherwise determines, common stock will be purchased for accounts of participating employees at a price per share equal to the lower of:

- 85% of the fair market value of a share on the first day of the offering; or

- 85% of the fair market value of a share on the purchase date.

For the first offering, which will begin on the effective date of this initial public offering, we will offer shares registered on a Form S-8 registration statement. Eligible employees will be permitted to authorize payroll deductions under the offering following the date on which the Form S-8 registration becomes effective. The fair market value of the shares on the first date of this offering will be the price per share at which our shares are first sold to the public as specified in the final prospectus with respect to our initial public offering. Otherwise, fair market value generally means the closing sales price (rounded up where necessary to the nearest whole cent) for such shares (or the closing bid, if no sales were reported) as quoted on the Nasdaq National Market on the trading day prior to the relevant determination date, as reported in The Wall Street Journal.

The board may provide that employees who become eligible to participate after the offering period begins nevertheless may enroll in the offering. These employees will purchase our stock at the lower of:

- 85% of the fair market value of a share on the day they began participating in the purchase plan; or

- 85% of the fair market value of a share on the purchase date.

If authorized by the board, participating employees may authorize payroll deductions of up to 15% of their compensation (including overtime pay, bonus, incentive pay and commissions) for the purchase of stock under the purchase

plan. Generally employees may end their participation in the offering at any time up to ten days before a purchase period ends. Their participation ends automatically on termination of their employment or loss of full-time status.

OTHER PROVISIONS

The board may grant eligible employees purchase rights under the purchase plan only if the purchase rights, together with any other purchase rights granted under other employee stock purchase plans established by us or by our affiliates, if any, do not permit the employee's rights to purchase our stock to accrue at a rate which exceeds $25,000 of fair market value of our stock for each calendar year in which the purchase rights are outstanding.

Upon a change in control, a surviving corporation may assume outstanding purchase rights or substitute other purchase rights therefor. If the surviving corporation does not assume or substitute the purchase rights, the participant's accumulated payroll deductions shall be used to purchase our stock immediately before the change in control and the participant's rights under the offering shall terminate following such purchase.

DESCRIPTION OF 401(K) PLAN

We maintain a retirement and deferred savings plan for our employees. The retirement and deferred savings plan is intended to qualify as a tax-qualified plan under Section 401 of the Internal Revenue Code. The retirement and deferred savings plan provides that each participant may contribute up to 20% of his or her pre-tax compensation (up to a statutory limit, which is $10,500 in calendar year 2000). Under the plan, each employee is fully vested in his or her deferred salary contributions. Employee contributions are held and invested by the plan's trustee. The retirement and deferred savings plan also permits us to make discretionary contributions, subject to established limits and a vesting schedule. To date, we have not made any discretionary contributions to the retirement and deferred savings plan on behalf of participating employees.

LIMITATIONS OF LIABILITY; INDEMNIFICATION OF DIRECTORS AND OFFICERS

In connection with the consummation of this offering, we will adopt and file an amended and restated certificate of incorporation and amended and restated bylaws. As permitted by Delaware law, our amended and restated certificate of incorporation provides that no director will be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director, except for liability:

- for any breach of duty of loyalty to us or to our stockholders;

- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;

- for unlawful payment of dividends or unlawful stock repurchases or redemptions under Section 174 of the Delaware General Corporation Law; or

- for any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation further provides that we must indemnify our directors to the fullest extent permitted by Delaware law.

In addition, our amended and restated bylaws provide that:

- we are required to indemnify our directors and officers to the fullest extent permitted by Delaware law, subject to limited exceptions;

- we may indemnify our other employees and agents to the extent that we indemnify our officers and directors, unless otherwise prohibited by law, our amended and restated certificate of incorporation, our amended and restated bylaws or agreements;

- we are required to advance expenses to our directors and executive officers as incurred in connection with legal proceedings against them for which they may be indemnified; and

- the rights conferred in the amended and restated bylaws are not exclusive.

We have entered into indemnification agreements with each of our directors and certain officers. These agreements, among other things, require us to indemnify each director and officer to the fullest extent permitted by Delaware law, including indemnification for expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or officer in any action or proceeding, including any action by or in the right of Rigel, arising out of the person's services as a director or officer of us, any subsidiary of ours or any other company or enterprise to which the person provides services at our request. At present, we are not aware of any pending or threatened litigation or proceeding involving any of our directors, officers, employees or agents in which indemnification would be required or permitted. We believe that our

charter provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers.

EMPLOYMENT AGREEMENTS

We have an employment agreement with Dr. Payan, dated as of January 16, 1997, and continuing indefinitely. Under the agreement, Dr. Payan is entitled to receive an annualized base salary of $185,000 and was issued 750,000 shares of our common stock. As of January 16, 2000, all such shares were fully vested and not subject to repurchase by us. Either Rigel or Dr. Payan may terminate his employment at any time for any reason. If we terminate Dr. Payan without cause, he will receive a severance payment equal to one year's base salary.

RELATED PARTY TRANSACTIONS

Stock option grants to our executive officers and directors are described in this prospectus under the heading "Management--Director Compensation, --Executive Compensation and - --Employment Agreements."

From January 31, 1997 through August 31, 2000, the following executive officers, directors and holders of more than 5% of our voting securities purchased securities in the amounts and as of the dates set forth below.

<TABLE>
<CAPTION>

EXECUTIVE OFFICERS, DIRECTORS AND 5% STOCKHOLDERS(1)	COMMON STOCK	PREFERRED STOCK					
		SERIES A	SERIES B	SERIES C	SERIES D	SERIES D WARRANTS	SERIES E
<S>	<C>	<C>	<C>	<C>	<C>	<C>	<C>
DIRECTORS							
Tak W. Mak(2)	50,000	--	--	--	--	--	--
Thomas S. Volpe	--	--	--	--	--	--	33,333
FIVE PERCENT STOCKHOLDERS							
Entities affiliated with Alta Partners(3)	--	--	2,500,000	1,403,509	558,107	55,640	166,667
Entities affiliated with Frazier and Company, Inc.(4)	--	--	--	3,649,123	521,596	52,000	125,000
Johnson & Johnson Development Corporation	--	--	--	--	1,500,000	--	166,666
Entities affiliated with Lombard Odier & Cie	--	--	3,750,000	2,105,263	837,161	83,460	500,000
Novartis Pharma AG	--	--	--	--	2,000,000	--	--
Price Per Share	$4.50		$.80	$1.14	$2.00	$2.00	$6.00
Date(s) of Purchase	1/00		1/97	11/97	12/98-5/99	12/98	2/00-8/00

</TABLE>

- --------------------------

(1) See "Principal Stockholders" for more detail on shares held by these purchasers.

(2) Dr. Mak resigned as a director on March 8, 2000.

(3) Dr. Deleage, one of our directors, is the managing general partner of Alta Partners.

(4) Mr. Frazier, one of our directors, is the managing principal of Frazier and Company, Inc.

Upon the closing of this offering, all shares of our outstanding preferred stock will automatically convert into shares of common stock on a one-for-one basis.

We have entered into an Amended and Restated Registration Rights Agreement with each of the purchasers of preferred stock set forth above, pursuant to which these and other stockholders will have registration rights with respect to their shares of common stock issuable upon conversion of their preferred stock following this offering.

We have entered into indemnification agreements with our directors and certain officers for the indemnification and advancement of expenses to these persons to the fullest extent permitted by law. We also intend to enter into those agreements with our future directors and officers.

In September 1999, we established a research collaboration and license agreement with Cell Genesys, Inc. James Gower, our President and Chief Executive Officer, serves on the board of directors of Cell Genesys. Stephen A. Sherwin, MD, who serves on our board of directors, is President, Chief Executive Officer and Chairman of the Board of Cell Genesys.

We anticipate that we will sell 1,111,111 shares of our common stock to Novartis in a private placement concurrent with this offering pursuant to our agreement with Novartis, dated May 26, 1999.

We believe that all of the transactions set forth above were made on terms no less favorable to us than could have been obtained from unaffiliated third parties. All future transactions, including loans, between us and our officers, directors, principal stockholders and their affiliates will be approved by a majority of our board of directors, including a majority of the independent and disinterested directors, and will be on terms no less favorable to us than could be obtained from unaffiliated third parties.

PRINCIPAL STOCKHOLDERS

The following table shows information known to us with respect to the beneficial ownership of our common stock as of August 31, 2000, and as adjusted to reflect the sale of the shares of common stock offered in the public offering under this prospectus and the concurrent private placement by:

- each person or group who beneficially owns more than 5% of our common stock;
- our chief executive officer;
- each of our four other most highly compensated executive officers whose compensation exceeded $100,000 during 1999;
- each of our directors; and
- all of our directors and executive officers as a group.

Beneficial ownership of shares is determined under the rules of the Securities and Exchange Commission and generally includes any shares over which a person exercises sole or shared voting or investment power. Except as indicated by footnote, and subject to applicable community property laws, each person identified in the table possesses sole voting and investment power with respect to all shares of common stock held by them. Shares of common stock subject to options currently exercisable or exercisable within 60 days of August 31, 2000 and not subject to repurchase as of that date are deemed outstanding for calculating the percentage of outstanding shares of the person holding these options, but are not deemed outstanding for calculating the percentage of any other person. Applicable percentage ownership in the following table is based on 29,424,419 shares of common stock outstanding as of August 31, 2000, assuming the conversion of all outstanding shares of preferred stock into common stock upon the closing of this offering, and 39,535,530 shares of common stock outstanding immediately following the completion of this offering, including the shares to be issued to Novartis in the concurrent private placement. Unless otherwise indicated, the address of each of the named individuals is c/o Rigel Pharmaceuticals, Inc., 240 East Grand Avenue, South San Francisco, California 94080.

<TABLE>
<CAPTION>

BENEFICIAL OWNER	SHARES OF COMMON STOCK OUTSTANDING	SHARES ISSUABLE PURSUANT TO OPTIONS EXERCISABLE WITHIN 60 DAYS OF AUGUST 31, 2000	PERCENT OF TOTAL OUTSTANDING BENEFICIALLY OWNED	
			PRIOR TO OFFERINGS	AFTER THE OFFERINGS
<S>	<C>	<C>	<C>	<C>

FIVE PERCENT STOCKHOLDERS			
Entities affiliated with Lombard Odier & Cie(1) 11. rue de la Corraterie 1211 Geneve 11 Switzerland	7,275,884	--	24.7% 18.4%
Entities affiliated with Alta Partners(2)... One Embarcadero Center, Suite 4050 San Francisco, CA 94111	4,683,923	--	15.9 11.9
Entities affiliated with Frazier and Company, Inc.(3) 601 Union Street, Suite 2110 Seattle, WA 98101	4,347,719	--	14.8 11.0
Novartis Pharma AG(4) Head Financial Investments CH-4002 Basil, Switzerland	3,111,111	--	10.6 7.9
Johnson & Johnson Development Corporation... One Johnson & Johnson Plaza New Brunswick, NJ 08933	1,666,666	--	5.7 4.2
DIRECTORS AND NAMED EXECUTIVE OFFICERS			
James M. Gower	500,000	150,000	2.2 1.6
Donald G. Payan	750,000	50,000	2.7 2.0
Brian C. Cunningham	100,000	162,500	* *
James H. Welch	37,500	14,375	* *
Donald W. Perryman(5)	--	75,000	* *
Jean Deleage(2)	4,683,923	--	15.9 11.9
Alan D. Frazier(3)	4,347,719	--	14.8 11.0
Walter H. Moos	--	12,777	* *
Stephen A. Sherwin	--	7,682	* *
Thomas S. Volpe	33,333	1,666	* *
All executive officers and directors as a group (11 people) (6)	10,452,475	474,000	37.1% 27.6%

- ---

* Less than one percent (1%).

(1) Includes 5,087,161 shares held by Lombard Odier & Cie and 2,105,263 shares held by Ryco and Co. Also includes 83,460 shares issuable upon the exercise of warrant within 60 days of August 31, 2000.

(2) Includes 4,579,305 shares held by Alta California Partners, L.P. and 104,618 shares held by Alta Embarcadero Partners, LLC. Dr. Deleage, a managing general partner of Alta Partners, disclaims beneficial ownership of the shares held by funds affiliated with Alta Partners except to the extent of his proportionate pecuniary interest therein.

(3) Includes 15,144 shares held by Frazier and Company, Inc. and 4,332,575 shares held by Frazier Healthcare II, L.P. Mr. Frazier, a managing principal of Frazier and Company, Inc., disclaims beneficial ownership of the shares held by Frazier and Company, Inc. and Frazier Healthcare II, L.P. except to the extent of his proportionate pecuniary interest therein.

(4) Includes the sale of 1,111,111 shares of common stock in a private placement concurrent with the closing of this initial public offering.

(5) Mr. Perryman resigned as Vice President, Business Development, effective January 15, 2000.

(6) Includes 83,460 shares issuable upon the exercise of a warrant that is exercisable within 60 days of August 31, 2000.

DESCRIPTION OF SECURITIES

Upon the closing of this offering and the filing of our amended and restated certificate of incorporation, our authorized capital stock will consist of 100,000,000 shares of common stock, $.001 par value, and 10,000,000 shares of preferred stock, $.001 par value.

COMMON STOCK

As of June 30, 2000, there were 29,148,229 shares of common stock outstanding that were held of record by approximately 151 stockholders after giving effect to the conversion of our preferred stock into common stock at a one-to-one ratio. There will be 39,259,340 shares of common stock outstanding (assuming no exercise of the underwriters' over-allotment option and no exercise of outstanding options) after giving effect to the sale of the shares of common stock offered by this prospectus and the concurrent private placement to Novartis.

The holders of common stock are entitled to one vote per share on all matters submitted to a vote of our stockholders and do not have cumulative voting rights. Accordingly, holders of a majority of the shares of common stock entitled to vote in any election of directors may elect all of the directors standing for election. Subject to preferences that may be applicable to any preferred stock outstanding at the time, the holders of outstanding shares of common stock are entitled to receive ratably any dividends out of assets legally available therefor as our board of directors may from time to time determine. Upon liquidation, dissolution or winding up of Rigel, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities and the liquidation preference of any then outstanding shares of preferred stock. Holders of common stock have no preemptive or conversion rights or other subscription rights. There are no redemption or sinking fund provisions applicable to the common stock. All outstanding shares of common stock are fully paid and nonassessable.

PREFERRED STOCK

Pursuant to our amended and restated certificate of incorporation, our board of directors will have the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock, in one or more series. Our board shall determine the rights, preferences, privileges and restrictions of the preferred stock, including dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. The issuance of preferred stock could adversely affect the voting power of holders of common stock, and the likelihood that holders of preferred stock will receive dividend payments and payments upon liquidation may have the effect of delaying, deferring or preventing a change in control of Rigel, which could depress the market price of our common stock. We have no preset plan to issue any shares of preferred stock.

WARRANTS

As of June 30, 2000, three warrants to purchase an aggregate of 150,000 shares of our common stock were outstanding. These warrants shall expire upon the earlier of (i) June 1, 2008 or (ii) seven years after the closing of the initial public offering of our stock and entitle the holders of these warrants to purchase up to 150,000 shares of our common stock at a price of $1.14 per share, subject to adjustment in the event of a merger, reorganization or sale of Rigel. These warrants give the holders the right of a net issue election.

As of June 30, 2000, one warrant to purchase 175,000 shares of our Series B preferred stock was outstanding. This warrant automatically converts upon the earlier of (i) April 30, 2004 or (ii) a merger or reorganization involving Rigel and entitles the holder of this warrant to purchase up to 175,000 shares of our Series B preferred stock at a price of $.80 per share, subject to adjustment in the event of a merger, reorganization or sale of Rigel. This warrant gives the holder the right of a net issue election.

As of June 30, 2000, one warrant to purchase 131,578 shares of our Series C preferred stock was outstanding. This warrant shall expire upon June 30, 2005 and entitles the holder of this warrant to purchase up to 131,578 shares of our Series C preferred stock at a price of $1.14 per share, subject to adjustment in the event of a merger, reorganization or sale of us. This warrant gives the holder the right of a net issue election.

As of June 30, 2000, one warrant to purchase an aggregate of 83,460 shares of our Series D preferred stock was outstanding. This warrant shall expire upon the earlier of (i) the closing of the initial public offering of our stock, (ii) a reorganization, merger or sale of Rigel or (iii) December 3, 2003 and entitle the holder of this warrant to purchase up to 83,460 shares of our Series D preferred stock at a price of $2.00 per share, subject to adjustment in the event of a merger, reorganization or sale of us. This warrant gives the

holder the right of a net issue election.

REGISTRATION RIGHTS

Upon completion of this offering and the concurrent private placement to Novartis, holders of an aggregate of 25,864,121 shares of common stock and warrants to purchase an aggregate of 306,578 shares of common stock will be entitled to rights to register these shares under the Securities Act. These rights are provided under an Amended and Restated Registration Rights Agreement, dated February 3, 2000, and under agreements with similar registration rights. If we propose to register any of our securities under the Securities Act, either for our own account or for the account of others, the holders of these shares are entitled to notice of the registration and are entitled to include, at our expense, their shares of common stock in the registration and any related underwriting, provided, among other conditions, that the underwriters may limit the number of shares to be included in the registration and in some cases, including this offering, exclude these shares entirely. In addition, the holders of these shares may require us, at our expense and on not more than two occasions at any time beginning six months from the date of the closing of this offering, to file a registration statement under the Securities Act with respect to their shares of common stock, and we will be required to use our best efforts to effect the registration. Further, the holders may require us at our expense to register their shares on Form S-3 when this form becomes available.

ANTI-TAKEOVER PROVISIONS OF CERTAIN PROVISIONS OF DELAWARE LAW AND OUR CHARTER CERTIFICATE ON
INCORPORATION AND BYLAWS

We are subject to Section 203 of the Delaware General Corporation Law. In general, the statute prohibits a publicly held Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless:

- prior to the date, our board of directors approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;

- upon consummation of the transaction that resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding those shares owned by persons who are directors and also officers, and by employee stock plans in which shares held subject to the plan will be tendered in a tender or exchange offer; or

- on or subsequent to this date, the business combination is approved by our board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

- Section 203 defines "business combination" to include:

- any merger or consolidation involving the corporation and the interested stockholder;

- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;

- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; and

- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

Our amended and restated certificate of incorporation requires that upon completion of the offering, any action required or permitted to be taken by our stockholders must be effected at a duly called annual or special meeting of stockholders and may not be effected by a consent in writing. Additionally, our amended and restated certificate of incorporation:

- substantially limits the use of cumulative voting in the election of directors;

- provides that the authorized number of directors may be changed only by resolution of our board of directors; and

- authorizes our board of directors to issue blank check preferred stock to increase the amount of outstanding shares.

Our amended and restated bylaws provide that candidates for director may be nominated only by our board of directors or by a stockholder who gives written notice to us no later than 60 days prior nor earlier than 90 days prior to the first anniversary of the last annual meeting of stockholders. The authorized number of directors is fixed in accordance with our amended and restated certificate of incorporation. Our board of directors may appoint new directors to fill vacancies or newly created directorships. Our amended and restated bylaws also limit who may call a special meeting of stockholders.

Upon completion of the offering, the terms of the board of directors will be divided into three classes each with a term of three years: Class I, whose term will expire at the annual meeting of stockholders to be held in 2001; Class II, whose term will expire at the annual meeting of stockholders to be held in 2002; and Class III, whose term will expire at the annual meeting of stockholders to be held in 2003. The Class I directors are Mr. Frazier and Dr. Deleage, the Class II directors are Dr. Moos, Dr. Sherwin and Mr. Volpe and the Class III directors are Mr. Gower and Dr. Payan. At each annual meeting of stockholders after the initial classification, the successors to directors whose terms expire will be elected to serve a term of three years. This classification of directors may have the effect of delaying or preventing changes in our control.

Delaware law and these charter provisions may have the effect of deterring hostile takeovers or delaying changes in control of our management, which could depress the market price of our common stock.

TRANSFER AGENT AND REGISTRAR

The transfer agent and registrar for the common stock is Wells Fargo Bank Minnesota, N.A.

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of substantial amounts of our common stock in the public market could adversely affect prevailing market prices. Furthermore, since no shares will be available for sale shortly after this offering because of contractual and legal restrictions on resale as described below, sales of substantial amounts of our common stock in the public market after these restrictions lapse could adversely affect the prevailing market price and our ability to raise equity capital in the future.

Upon completion of this offering and the concurrent private placement to Novartis, we will have outstanding an aggregate of 39,535,530 shares of common stock, assuming no exercise of the underwriters' over-allotment option and no exercise of outstanding options or warrants after August 31, 2000. Of these shares, all of the shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act, unless these shares are purchased by affiliates. The remaining 30,535,530 shares of common stock held by existing stockholders are restricted securities. Restricted securities may be sold in the public market only if registered or if they qualify for an exemption from registration described below under Rules 144, 144(k) or 701 promulgated under the Securities Act.

As a result of the contractual restrictions described below and the provisions of Rules 144, 144(k) and 701, the restricted shares will be available for sale in the public market as follows:

- no shares will be eligible for sale upon completion of this offering;

- 29,391,086 shares will be eligible for sale upon the expiration of the lock-up agreements, described below, beginning 180 days after the date of this prospectus; and

- 1,881,853 shares will be eligible for sale upon the exercise of vested options 180 days after the date of this prospectus.

LOCK-UP AGREEMENTS

All of our officers, directors and stockholders and option holders have agreed not to transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into shares or exercisable or exchangeable for shares of our common stock, for a period of at least 180 days after the date of this prospectus. Transfers or dispositions can be made sooner only with the prior written consent of Morgan Stanley Dean Witter. Morgan Stanley & Co. Incorporated may release any of the shares subject to these lock-up agreements at any time without notice.

RULE 144

In general, under Rule 144 as currently in effect, beginning 90 days after

the date of this prospectus, a person or persons whose shares are aggregated, who has beneficially owned restricted securities for at least one year, including the holding period of any prior owner except an affiliate, would be entitled to sell within any three-month period a number of shares that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately 395,355 shares immediately after this offering; or

- the average weekly trading volume of our common stock on the Nasdaq National Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Sales under Rule 144 are also subject to manner of sale provisions and notice requirements and to the availability of current public information about Rigel.

RULE 144(K)

Under Rule 144(k), a person who is not deemed to have been one of our affiliates at any time during the 90 days preceding a sale, and who has beneficially owned the shares proposed to be sold for at least two years, including the holding period of any prior owner except an affiliate, is entitled to sell these shares without complying with the manner of sale, public information, volume limitation or notice provisions of Rule 144. 4,727,059 shares of our common stock will qualify as "144(k) shares" within 180 days after the date of this prospectus.

RULE 701

In general, under Rule 701 of the Securities Act as currently in effect, any of our employees, consultants or advisors, other than affiliates, who purchase or receive shares from us in connection with a compensatory stock purchase plan or option plan or other written agreement will be eligible to resell their shares beginning 90 days after the date of this prospectus, subject only to the manner of sale provisions of Rule 144, and by affiliates under Rule 144 without compliance with its holding period requirements.

REGISTRATION RIGHTS

Upon completion of this offering and the concurrent private placement to Novartis, the holders of an aggregate of 25,864,121 of our common stock and warrants to purchase an aggregate of 306,578 shares of common stock, or their transferees, will be entitled to rights with respect to the registration of their shares under the Securities Act. Registration of their shares under the Securities Act would result in these shares becoming freely tradeable without restriction under the Securities Act, except for shares purchased by affiliates, immediately upon the effectiveness of such registration.

STOCK OPTIONS

Following this offering, we intend to file a registration statement on Form S-8 under the Securities Act covering the shares of common stock reserved for issuance under our 2000 Equity Incentive Plan, 2000 Employee Stock Purchase Plan and 2000 Non-Employee Directors' Stock Option Plan that will become effective upon filing. Accordingly, shares registered under that registration statement will, subject to Rule 144 volume limitations applicable to affiliates, be available for sale in the open market after the filing, except those shares subject to lock-up agreements.

UNDERWRITERS

Under the terms and subject to the conditions contained in the underwriting agreement dated the date hereof, the underwriters named below, for whom Morgan Stanley & Co. Incorporated, Lehman Brothers Inc. and FleetBoston Robertson Stephens, Inc. are acting as representatives, have severally agreed to purchase, and Rigel has agreed to sell to them, an aggregate of 9,000,000 shares of common stock. The number of shares of common stock that each underwriter has agreed to purchase is set forth opposite its name below:

<TABLE>
<CAPTION>

UNDERWRITERS	NUMBER OF SHARES
<S>	<C>
Morgan Stanley & Co. Incorporated.....	
Lehman Brothers Inc.....	
Robertson Stephens, Inc.....	
Total.....	9,000,000

</TABLE>

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered hereby are subject to the approval of certain legal matters by their counsel and to certain other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered hereby, other than those covered by the over-allotment option described below, if any such shares are taken.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the public offering price set forth on the cover page hereof and part to certain dealers at a price that represents a concession not in excess of $ a share under the public offering price. Any underwriters may allow, and such dealers may reallow, a concession not in excess of $ a share to other underwriters or to certain other dealers. After the offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives of the underwriters.

Rigel has granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 1,350,000 additional shares of common stock at the public offering price set forth on the cover page hereof, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with this offering of common stock. To the extent this option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase approximately the same percentage of additional shares of common stock as the number set forth next to the underwriter's name in the preceding table bears to the total number of shares of common stock set forth next to the names of all underwriters in the preceding table. The following table provides information regarding the amount of the discount to be paid by us to the underwriters:

<TABLE>
<CAPTION>

		TOTAL	
		WITHOUT	WITH
	PER SHARE	OVER-ALLOTMENT	OVER-ALLOTMENT
<S>	<C>	<C>	<C>
Underwriting discounts and commissions to be paid by us	$	$	$

</TABLE>

We estimate that the total expenses of the offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding underwriting discounts and commissions, will be approximately $1 million.

Rigel, our directors and officers and certain other stockholders have each agreed, without the prior written consent of Morgan Stanley & Co. Incorporated on behalf of the underwriters, during the period ending 180 days after the date of this prospectus, subject to certain exceptions, not to, directly or indirectly:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of common stock or any securities convertible into or exercisable or exchangeable for common stock, or

- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of common stock,

whether any such transaction described above is to be settled by delivery of common stock or such other securities, in cash or otherwise. The foregoing restrictions shall not apply to (1) the sale of any shares to the underwriters, (2) transactions relating to shares of our common stock (other than shares acquired in the directed share program) or other securities acquired in open market transactions after the date of this prospectus or (3) the transfer of shares of common stock or any securities convertible into or exercisable or exchangeable for common stock to a member of the stockholder's immediate family or to a trust of which the stockholder or an immediate family member is the beneficiary if certain conditions are met. Morgan Stanley & Co. Incorporated may release any of the shares subject to these lock-up agreements at any time without notice.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed five percent of the total number of shares of common stock offered by them.

Our common stock will be quoted on the Nasdaq National Market under the symbol "RIGL."

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may over-allot in connection with the offering, creating a short position in the common stock for their own account. In addition, to cover over-allotments or to stabilize the price of the common stock, the underwriters may bid for, and purchase, shares of common stock in the open market. Finally, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the common stock in the offering if the syndicate repurchases previously distributed shares of common stock in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize or maintain the market price of the common stock above independent market levels. The underwriters are not required to engage in these activities and may end any of these activities at any time.

The underwriting agreement provides that Rigel and the underwriters will indemnify each other against certain liabilities, including liabilities under the Securities Act.

DIRECTED SHARE PROGRAM PROSPECTUS DISCLOSURE

At the request of Rigel, the underwriters have reserved for sale at the initial offering price, up to 450,000 shares in this offering for directors, officers, employees, business associates and related persons of Rigel. The shares of common stock available for sale to the general public will be reduced to the extent such persons purchase such reserved shares. Any reserved shares which are not so purchased will be offered by the underwriters to the general public on the same basis as the other shares in this offering.

PRICING OF THE OFFERING

Prior to this offering, there has been no public market for the securities. The initial public offering price will be determined by negotiations between Rigel and the underwriters. Among the factors to be considered in determining the initial public offering price will be the future prospects of Rigel and its industry in general, sales, earnings and certain other financial and operating information of Rigel in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities and certain financial and operating information of companies engaged in activities similar to those of Rigel. The estimated initial public offering price range set forth on the cover page of this prospectus is subject to change as a result of market conditions and other factors.

LEGAL MATTERS

Cooley Godward LLP, Palo Alto, California, will provide us with an opinion as to the validity of the common stock offered under this prospectus. Skadden, Arps Slate, Meagher & Flom LLP, will pass upon certain legal matters related to this offering for the underwriters. As of the date of this prospectus, certain partners and associates of Cooley Godward LLP own an aggregate of 78,860 shares of our common stock through investment partnerships. Brian Cunningham, our Senior Vice President, Chief Operating Officer, Chief Financial Officer and Secretary, is Of Counsel with Cooley Godward and participates in their investment partnerships. Mr. Cunningham currently holds 100,000 shares of our common stock and holds options to purchase 600,000 shares of our common stock.

EXPERTS

Ernst & Young LLP, independent auditors, have audited our financial statements at December 31, 1998 and December 31, 1999, and for the years ended December 31, 1997, 1998 and 1999, as set forth in their report. We have included our financial statements in this prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission (the "SEC") a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered under this prospectus. This prospectus does not contain all of the information in the registration statement and the exhibits and schedule to the registration statement. For further information with respect to us and our common stock, we refer you to the registration statement and to the exhibits and schedule to registration statement. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference. You may inspect a copy of the registration statement without charge at the SEC's principal office in Washington, D.C., and copies of all or

any part of the registration statement may be obtained from the Public Reference Section of the SEC, 450 Fifth Street, N.W., Washington, D.C. 20549, upon payment of fees prescribed by the SEC. The SEC maintains a World Wide Web site that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address of the Web site is http://www.sec.gov. The SEC's toll free investor information service can be reached at 1-800-SEC-0330. Information contained on our website does not constitute part of this prospectus.

Upon completion of the offering, we will be subject to the information reporting requirements of the Securities Exchange Act of 1934, as amended, and we will file reports, proxy statements and other information with the SEC.

We intend to furnish our stockholders with annual reports containing financial statements audited by our independent public accountants and quarterly reports for the first two fiscal quarters of each fiscal year containing unaudited interim financial information. Our telephone number is (650) 624-1100.

RIGEL PHARMACEUTICALS, INC.
INDEX TO FINANCIAL STATEMENTS

<TABLE>
<CAPTION>

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REPORT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

The Board of Directors
Rigel Pharmaceuticals, Inc.

We have audited the accompanying balance sheets of Rigel Pharmaceuticals, Inc. as of December 31, 1998 and 1999, and the related statements of operations, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 1999. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Rigel Pharmaceuticals, Inc. at December 31, 1998 and 1999, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 1999 in conformity with accounting principles generally accepted in the United States.

/s/ Ernst & Young LLP

Palo Alto, California
February 25, 2000

RIGEL PHARMACEUTICALS, INC.

BALANCE SHEETS

(IN THOUSANDS, EXCEPT SHARE AND PER SHARE AMOUNTS)

<TABLE>
<CAPTION>

	PRO FORMA

	DECEMBER 31,		JUNE 30,	STOCKHOLDERS' EQUITY AT JUNE 30,
	1998	1999	2000	2000
				(UNAUDITED)
<S>	<C>	<C>	<C>	<C>
ASSETS				
Current assets:				
Cash and cash equivalents	$ 9,493	$ 5,836	$ 15,694	
Accounts receivable	--	2,348	317	
Prepaid expenses and other current assets	112	346	504	
Total current assets	9,605	8,530	16,515	
Property and equipment, net	3,218	8,398	8,770	
Other assets	133	241	231	
	$ 12,956	$ 17,169	$ 25,516	
LIABILITIES AND STOCKHOLDERS' EQUITY				
Current liabilities:				
Accounts payable	$ 484	$ 883	$ 1,388	
Accrued compensation	104	288	363	
Accrued liabilities	916	1,403	808	
Deferred revenue	2,833	4,770	2,874	
Capital lease obligations	721	2,176	2,502	
Total current liabilities	5,058	9,520	7,935	
Capital lease obligations	1,652	5,478	5,121	
Long-term portion of deferred revenue	639	956	455	
Other long-term liabilities	162	459	747	
Commitments				
Stockholders' equity:				
Convertible preferred stock, $0.001 par value; 22,000,000, 24,000,000 and 26,750,000 shares authorized in 1998, 1999 and June 30, 2000, respectively (none pro forma), issuable in series; 19,033,707, 22,053,887 and 24,719,677 shares issued and outstanding in 1998, 1999 and June 30, 2000, respectively (none pro forma); (aggregate liquidation preference of $27,475 at 1999 and $43,037 at June 30, 2000)	19	22	25	$ --
Common stock, $0.001 par value; 35,000,000 shares authorized in 1998, 37,500,000 shares authorized in 1999 and June 30, 2000, (100,000,000 shares pro forma); 2,675,333, 3,095,834 and 4,428,552 shares issued and outstanding in 1998, 1999 and June 30, 2000, respectively (29,148,229 shares pro forma)	3	3	4	29
Additional paid-in capital	21,676	35,164	55,982	55,982
Deferred stock compensation	--	(5,814)	(5,333)	(5,333)
Accumulated deficit	(16,253)	(28,619)	(39,420)	(39,420)
Total stockholders' equity	5,445	756	11,258	$ 11,258
	$ 12,956	$ 17,169	$ 25,516	

</TABLE>

See accompanying notes.

RIGEL PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS

(IN THOUSANDS, EXCEPT PER SHARE AMOUNTS)

<TABLE>
<CAPTION>

	YEARS ENDED DECEMBER 31,			SIX MONTHS ENDED JUNE 30,	
	1997	1998	1999	1999	2000
				(UNAUDITED)	
<S>	<C>	<C>	<C>	<C>	<C>
Contract revenues from collaborations	$ --	$ 28	$ 8,984	$ 3,069	$ 6,797
Costs and expenses:					
Research and development (see Note A)	4,568	8,305	17,112	6,830	14,636
General and administrative (see Note A)	1,033	2,217	3,952	1,708	2,994

Total costs and expenses.....	5,601	10,522	21,064	8,538	17,630
Loss from operations.....	(5,601)	(10,494)	(12,080)	(5,469)	(10,833)
Interest income (expense), net.....	85	(110)	(286)	12	32
Net loss.....	$(5,516)	$(10,604)	$(12,366)	$(5,457)	$(10,801)
Net loss per share, basic and diluted.....	$ (2.20)	$ (4.01)	$ (4.39)	$ (2.02)	$ (2.60)
Weighted average shares used in computing net loss per share, basic and diluted.....	2,512	2,643	2,818	2,703	4,162
Pro forma net loss per share, basic and diluted (unaudited).....			$ (0.52)		$ (0.38)
Weighted average shares used in computing pro forma net loss per share, basic and diluted (unaudited).....			23,996		28,393

- ------------------------

Note A:

Includes charges for stock-based compensation as follows:

Research and development.....	$ --	$ 6	$ 2,321	$ 163	$ 4,245
General and administrative.....	$ --	$ --	$ 254	$ 41	$ 396

See accompanying notes.

RIGEL PHARMACEUTICALS, INC.

STATEMENT OF STOCKHOLDERS' EQUITY
(IN THOUSANDS, EXCEPT SHARE AND PER SHARE AMOUNTS)

	CONVERTIBLE PREFERRED STOCK		COMMON STOCK		ADDITIONAL PAID-IN	DEFERRED STOCK	ACCUMULATED
	SHARES	AMOUNT	SHARES	AMOUNT	CAPITAL	COMPENSATION	DEFICIT
Balance at December 31, 1996.....	665,000	1	2,400,000	3	58	--	(133)
Issuance of common stock at $0.001 per share for cash in January 1997.....	--	--	110,000	--	--	--	--
Issuance of Series B convertible preferred stock at $0.80 per share in January 1997 for cash, net of issuance cost.....	7,500,000	8	--	--	5,961	--	--
Issuance of warrants to purchase Series B preferred stock for financing arrangement.....	--	--	--	--	47	--	--
Issuance of Series C preferred stock at $1.14 per share in November 1997 for cash, net of issuance cost.....	7,236,843	7	--	--	8,202	--	--
Issuance of Series C preferred stock at $1.14 per share in August 1997 for license rights.....	150,000	--	--	--	171	--	--
Issuance of options to consultants for services.....	--	--	--	--	5	--	--
Issuance of common stock upon exercise of options.....	--	--	46,667	--	5	--	--

Net loss and comprehensive loss... (5,516)	--	--	--	--	--	--	
	19,033,707	19	2,675,333	3	21,676	--	
Balance at December 31, 1997..... (5,649)	15,551,843	16	2,556,667	3	14,449	--	
Issuance of warrants to purchase Series C preferred stock for financing arrangement..... --	--	--	--	--	86	--	
Issuance of Series D preferred stock at $2.00 per share in December 1998 for cash, net of issuance costs..... --	3,481,864	3	--	--	6,938	--	
Issuance of warrants to purchase Series D preferred stock for financing arrangement..... --	--	--	--	--	185	--	
Compensation expense related to options granted to consultants..... --	--	--	--	--	6	--	
Issuance of common stock upon exercise of options..... --	--	--	118,666	--	12	--	
Net loss and comprehensive loss... (10,604)	--	--	--	--	--	--	
	19,033,707	19	2,675,333	3	21,676	--	
Balance at December 31, 1998..... (16,253)							

<CAPTION>

	TOTAL STOCKHOLDERS' EQUITY
<S>	<C>
Balance at December 31, 1996.....	(71)
Issuance of common stock at $0.001 per share for cash in January 1997.....	--
Issuance of Series B convertible preferred stock at $0.80 per share in January 1997 for cash, net of issuance cost.....	5,969
Issuance of warrants to purchase Series B preferred stock for financing arrangement.....	47
Issuance of Series C preferred stock at $1.14 per share in November 1997 for cash, net of issuance cost.....	8,209
Issuance of Series C preferred stock at $1.14 per share in August 1997 for license rights.....	171
Issuance of options to consultants for services.....	5
Issuance of common stock upon exercise of options.....	5
Net loss and comprehensive loss...	(5,516)
Balance at December 31, 1997.....	8,819
Issuance of warrants to purchase Series C preferred stock for financing arrangement.....	86
Issuance of Series D preferred stock at $2.00 per share in December 1998 for cash, net of issuance costs.....	6,941
Issuance of warrants to purchase Series D preferred stock for financing arrangement.....	185
Compensation expense related to options granted to consultants.....	6
Issuance of common stock upon exercise of options.....	12
Net loss and comprehensive loss...	(10,604)
Balance at December 31, 1998.....	5,445

</TABLE>

(TABLE CONTINUED ON FOLLOWING PAGE.)

STATEMENT OF STOCKHOLDERS' EQUITY (CONTINUED)
(IN THOUSANDS, EXCEPT SHARE AND PER SHARE AMOUNTS)

<TABLE>
<CAPTION>

	CONVERTIBLE PREFERRED STOCK		COMMON STOCK		ADDITIONAL PAID-IN	DEFERRED STOCK	ACCUMULATED
	SHARES	AMOUNT	SHARES	AMOUNT	CAPITAL	COMPENSATION	DEFICIT
<S>	<C>	<C>	<C>	<C>	<C>	<C>	<C>
Issuance of Series C preferred stock at $1.14 per share for financing arrangement.....	20,000	--	--	--	23	--	--
Issuance of Series D preferred stock at $2.00 per share for cash, net of issuance cost.....	3,000,000	3	--	--	5,925	--	--
Issuance of Series D preferred stock upon exercise of warrant at $2.00 per share.....	180	--	--	--	--	--	--
Issuance of common stock upon exercise of options.....	--	--	420,501	--	51	--	--
Compensation expense related to options granted to consultants.....	--	--	--	--	406	--	--
Deferred stock compensation.....	--	--	--	--	7,083	(7,083)	--
Amortization of deferred stock compensation.....	--	--	--	--	--	1,269	--
Net loss and comprehensive loss.....	--	--	--	--	--		(12,366)
Balance at December 31, 1999.....	22,053,887	22	3,095,834	3	35,164	(5,814)	(28,619)
Issuance of Series E preferred stock at $6.00 per share for cash, net of issuance cost (unaudited).....	2,508,330	3	--	--	15,047	--	--
Issuance of Series E preferred stock in exchange for a technology license (unaudited).....	50,000	--	--	--	300	--	--
Issuance of Series D preferred stock upon exercise of warrant at $2.00 per share (unaudited).....	107,460	--	--	--	215	--	--
Issuance of common stock upon exercise of options (unaudited).....	--	--	1,232,718	1	196	--	
Issuance of common stock for services.....	--	--	100,000	--	450	--	--
Compensation expense related to options granted to consultants (unaudited).....	--	--	--	--	3,109	--	--
Deferred stock compensation (unaudited).....	--	--	--	--	1,501	(1,501)	--
Amortization of deferred stock compensation (unaudited).....	--	--	--	--	--	1,982	--
Net loss and comprehensive loss (unaudited).....	--	--	--	--	--	--	(10,801)

Balance at June 30, 2000 (unaudited)	24,719,677	$ 25	4,428,552	$ 4	$55,982	$(5,333)
	$(39,420)					

<CAPTION>

	TOTAL STOCKHOLDERS' EQUITY
<S>	<C>
Issuance of Series C preferred stock at $1.14 per share for financing arrangement	23
Issuance of Series D preferred stock at $2.00 per share for cash, net of issuance cost	5,928
Issuance of Series D preferred stock upon exercise of warrant at $2.00 per share	--
Issuance of common stock upon exercise of options	51
Compensation expense related to options granted to consultants	406
Deferred stock compensation	--
Amortization of deferred stock compensation	1,269
Net loss and comprehensive loss	(12,366)
Balance at December 31, 1999	756
Issuance of Series E preferred stock at $6.00 per share for cash, net of issuance cost (unaudited)	15,050
Issuance of Series E preferred stock in exchange for a technology license (unaudited)	300
Issuance of Series D preferred stock upon exercise of warrant at $2.00 per share (unaudited)	215
Issuance of common stock upon exercise of options (unaudited)	197
Issuance of common stock for services	450
Compensation expense related to options granted to consultants (unaudited)	3,109
Deferred stock compensation (unaudited)	--
Amortization of deferred stock compensation (unaudited)	1,982
Net loss and comprehensive loss (unaudited)	(10,801)
Balance at June 30, 2000 (unaudited)	$ 11,258

</TABLE>

See accompanying notes.

RIGEL PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS

(IN THOUSANDS)

<TABLE>
<CAPTION>

	YEARS ENDED DECEMBER 31,			SIX MONTHS ENDED JUNE 30,	
	1997	1998	1999	1999	2000
					(UNAUDITED)
<S>	<C>	<C>	<C>	<C>	<C>

OPERATING ACTIVITIES					
Net loss	$(5,516)	$(10,604)	$(12,366)	$(5,457)	$(10,801)
Adjustments to reconcile net loss to net cash used in operating activities:					
Depreciation and amortization	409	1,103	1,906	769	1,213
Stock compensation expense	--	--	1,675	204	5,091
Issuances of equity instruments for noncash benefits	230	192	23	23	300
Changes in assets and liabilities:					
Accounts receivable	--	--	(2,348)	(1,150)	2,031
Prepaid expenses and other current assets	(104)	(9)	(234)	(163)	(158)
Other assets	(149)	17	(108)	(12)	10
Accounts payable	176	234	399	552	505
Accrued compensation	44	60	184	41	75
Accrued liabilities	412	503	487	(346)	(145)
Deferred revenue	--	3,472	2,254	1,256	(2,397)
Long-term liabilities	200	(39)	297	(86)	288
Net cash used in operating activities	(4,298)	(5,071)	(7,831)	(4,369)	(3,988)
INVESTING ACTIVITIES					
Capital expenditures	(2,341)	(2,389)	(7,086)	(6,082)	(1,585)
Net cash used in investing activities	(2,341)	(2,389)	(7,086)	(6,082)	(1,585)
FINANCING ACTIVITIES					
Proceeds from capital lease financing	1,847	1,427	6,696	4,073	1,044
Principal payments on capital lease obligations	(242)	(571)	(1,415)	(526)	(1,075)
Net proceeds from issuances of common stock	5	12	51	8	197
Net proceeds from issuances of convertible preferred stock	14,171	6,941	5,928	5,978	15,265
Net cash provided by financing activities	15,781	7,809	11,260	9,533	15,431
Net increase (decrease) in cash and cash equivalents	9,142	349	(3,657)	(918)	9,858
Cash and cash equivalents at beginning of period	2	9,144	9,493	9,493	5,836
Cash and cash equivalents at end of period	$ 9,144	$ 9,493	$ 5,836	$ 8,575	$ 15,694
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION					
Interest paid	$ 71	$ 161	$ 597	$ 154	$ 455
SCHEDULE OF NON CASH TRANSACTIONS					
Deferred stock compensation	$ --	$ --	$ 7,083	$ 2,311	$ 1,501

</TABLE>

See accompanying notes.

NOTES TO FINANCIAL STATEMENTS

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

NATURE OF OPERATIONS AND BASIS OF PRESENTATION

Rigel Pharmaceuticals, Inc. ("Rigel" or the "Company") was incorporated in the state of Delaware on June 14, 1996. The Company is engaged in the discovery and development of a broad range of new small molecule drug candidates.

The Company's current operating plan anticipates that the Company will require additional capital to fund its operations and continue its research and development programs. As of December 31, 1999, the Company has funded its operations primarily through the sale of private equity securities, payments from corporate collaborators and capital asset lease financings. The Company plans to seek additional funding through public or private financing arrangements with third parties.

USE OF ESTIMATES

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from these estimates.

INTERIM FINANCIAL INFORMATION

The financial information at June 30, 2000 and for the six months ended June 30, 1999 and 2000 is unaudited but, in the opinion of management, has been prepared on the same basis as the annual financial statements and includes all adjustments (consisting only of normal recurring adjustments) that the Company considers necessary for a fair presentation of the financial position at such date and the operating results and cash flow for such periods. Results for the six months ended June 30, 2000 are not necessarily indicative of the results to expected for any subsequent period.

UNAUDITED PRO FORMA INFORMATION

If the Company's initial public offering ("IPO") as described in Note 8 is consummated, all of the preferred stock outstanding will automatically be converted into common stock. The unaudited pro forma stockholders' equity at June 30, 2000 has been adjusted for the assumed conversion of preferred stock based on the shares of preferred stock outstanding at June 30, 2000.

CASH AND CASH EQUIVALENTS

The Company considers all highly liquid investments with an original maturity of 90 days or less, when purchased, to be cash equivalents. For the periods presented, cash equivalents consist of money market funds. The Company has established guidelines regarding diversification of its investments and their maturities that should maintain safety and liquidity.

FAIR VALUE OF FINANCIAL INSTRUMENTS

Financial instruments, including cash and cash equivalents, accounts receivable, accounts payable, accrued liabilities and accrued compensation are carried at cost, which management believes approximates fair value.

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)
PROPERTY AND EQUIPMENT

Property and equipment are stated at cost. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, which range from three to seven years. Leasehold improvements are amortized using the straight-line method over the estimated useful lives of the assets or the term of the lease, whichever is shorter.

REVENUE RECOGNITION

Non-refundable up-front payments received in connection with research and development collaboration agreements, including technology access fees, are deferred and recognized on a straight-line basis over the relevant periods specified in the agreement, generally the research term.

Revenue related to collaborative research with the Company's corporate collaborators are recognized as research services are performed over the related funding periods for each contract. Under these agreements, the Company is required to perform research and development activities as specified in each respective agreement. The payments received under each respective agreement are not refundable and are generally based on a contractual cost per full-time equivalent employee working on the project. Research and development expenses under the collaborative research agreements approximate or exceed the revenue recognized under such agreements over the term of the respective agreements. Deferred revenue may result when the Company does not incur the required level of effort during a specific period in comparison to funds received under the respective contracts. Milestone and royalty payments, if any, will be recognized pursuant to collaborative agreements upon the achievement of specified milestones.

RESEARCH AND DEVELOPMENT

Research and development expenditures, including direct and allocated expenses, are charged to expense as incurred. Collaboration agreements generally specify minimum levels of research effort required to be performed by the Company.

COMPREHENSIVE LOSS

Statement of Financial Accounting Standard No. 130, "Reporting Comprehensive Income" ("SFAS 130") requires components of other comprehensive income, including gains and losses on available-for-sale investments, to be included as part of total comprehensive income. For all periods presented, the comprehensive loss is equal to the net loss and has been disclosed in the statement of stockholders' equity.

IMPAIRMENT OF LONG-LIVED ASSETS

In accordance with the provisions of Statement of Financial Accounting Standards No. 121, "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to be Disposed Of" ("SFAS 121"), the Company reviews long-lived assets, including property and equipment, for impairment whenever events or changes in business circumstances indicate that the carrying amount of the assets may not be fully recoverable. Under SFAS 121, an impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition is

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)
less than its carrying amount. Impairment, if any, is assessed using discounted cash flows. Through June 30, 2000, there have been no such losses.

SEGMENT REPORTING

Statement of Financial Accounting Standards No. 131, "Disclosure about Segments of an Enterprise and Related Information" ("SFAS 131") establishes annual and interim reporting standards for an enterprise's operating segments and related disclosures about its products, services, geographic areas, and major customers. The Company has determined that it operates in only one segment. Accordingly, the adoption of SFAS 131 had no impact on the Company's financial statements.

ACCOUNTING FOR STOCK-BASED COMPENSATION

As permitted by Statement of Financial Accounting Standards No. 123, "Accounting for Stock-Based Compensation" ("SFAS 123"), the Company has elected to follow Accounting Principles Board Opinion No. 25, "Accounting for Stock Issued to Employees" and related interpretations in accounting for its employee stock option grants ("APB 25") and to disclose the pro forma effect of SFAS 123 (see Note 6). Pro forma net loss information, as required by ("SFAS 123"), is included in Note 6. Options granted to consultants are accounted for using the Black-Scholes method prescribed by SFAS 123 and in accordance with Emerging Issues Task Force Consensus No. 96-18 ("EITF 96-18") the options are subject to periodic re-valuation over their vesting terms.

NET LOSS PER SHARE

Net loss per share has been computed according to the Financial Accounting Standards Board Statement No. 128, "Earnings Per Share," which requires disclosure of basic and diluted earnings per share. Basic earnings per share excludes any dilutive effects of options, shares subject to repurchase, warrants, and convertible securities. Diluted earnings per share includes the impact of potentially dilutive securities. Following the guidance given by the Securities and Exchange Commission Staff Accounting Bulletin No. 98, common stock and preferred stock that has been issued or granted for nominal consideration prior to the anticipated effective date of the initial public offering must be included in the calculation of basic and diluted net loss per common share as if these shares had been outstanding for all periods presented. To date, the Company has not issued or granted shares for nominal consideration.

Pro forma net loss per share includes shares issuable upon the conversion of outstanding shares of preferred stock (using the as if method) from the original date of issuance.

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)
A reconciliation of shares used in the calculations is as follows (in thousands):

<TABLE>
<CAPTION>

	YEARS ENDED DECEMBER 31,			SIX MONTHS ENDED JUNE 30,	
	1997	1998	1999	1999	2000
				(UNAUDITED)	
<S>	<C>	<C>	<C>	<C>	<C>
Basic and diluted:					
Weighted-average shares of common stock outstanding....	2,512	2,643	2,818	2,703	4,162
Adjustment to reflect weighted-average effect of assumed conversions of preferred stock (unaudited)...			21,178		24,231
Weighted-average shares used in pro forma net loss per share, basic and diluted (unaudited).....			23,996		28,393

</TABLE>

During all periods presented, the Company had securities outstanding, which could potentially dilute basic earnings per share in the future, but were excluded from the computation of diluted net loss per share, as their effect would have been antidilutive. These outstanding securities consist of the following (in thousands):

<TABLE>
<CAPTION>

	YEARS ENDED DECEMBER 31,			SIX MONTHS ENDED JUNE 30,	
	1997	1998	1999	1999	2000
				(UNAUDITED)	
<S>	<C>	<C>	<C>	<C>	<C>
Convertible preferred stock.....	15,552	19,034	22,054	22,054	24,719
Outstanding options.....	1,475	3,354	5,242	4,581	5,159
Warrants.....	175	648	647	648	540

</TABLE>

SOFTWARE COSTS

In 1999, the Company adopted Statement of Position 98-1 ("SOP 98-1"), "ACCOUNTING FOR THE COSTS OF COMPUTER SOFTWARE DEVELOPED OR OBTAINED FOR INTERNAL USE". SOP 98-1 requires the capitalization of direct costs incurred in connection with developing or obtaining software for internal-use, including external direct costs of materials and services and payroll and payroll-related costs for employees who are directly associated with and devote time to an internal use software development project. The Company's policy is to capitalize all such costs and include them as computers and software to be amortized over their estimated useful lives. Through June 30, 2000, the Company had no costs related to the implementation of internal-use software.

RECENT ACCOUNTING PRONOUNCEMENTS

In June 1998, the Financial Accounting Standards Board ("FASB") issued statement of Financial Accounting Standards No. 133, "ACCOUNTING FOR DERIVATIVE FINANCIAL INSTRUMENTS AND FOR HEDGING ACTIVITIES" ("SFAS 133") which provides a comprehensive and consistent standard for the recognition and measurement of derivatives and hedging activities. In June 1999, FASB issued Financial Accounting Standards No. 137 which deferred the effective date of SFAS 133 to fiscal years beginning after June 15, 2000. The adoption of SFAS 133 is not anticipated to have an impact on the Company's results of

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)
operations of financial condition when adopted as the Company holds no derivative financial instruments and does not currently engage in hedging activities.

In December 1999, the Securities and Exchange Commission issued Staff Accounting Bulletin No. 101 ("SAB 101"). SAB 101 summarizes the SEC's views in applying generally accepted accounting principles to revenue recognition. The adoption of SAB 101 had no significant impact on the Company's revenue recognition policy or results of operations.

In March 2000, the FASB issued No. 44 ("FIN 44"), "Accounting for Certain Transactions Involving Stock compensation--an Interpretation of APB 25." This Interpretation clarifies (a) the definition of employee for purposes of applying Opinion 25, (b) the criteria for determining whether a plan qualifies as a noncompensatory plan, (c) the accounting consequence of various modifications to

the terms of a previously fixed stock option or award, and (d) the accounting for an exchange of stock compensation awards in a business combination. This Interpretation is effective July 1, 2000, but certain conclusions in this Interpretation cover specific events that occur after either December 15, 1998, or January 12, 2000. To the extent that this interpretation covers events occurring during the period after December 15, 1998, or January 12, 2000, but before the effective date of July 1, 2000, the effects of applying this Interpretation are recognized on a prospective basis from July 1, 2000. The adoption of FIN 44 does not have a material impact on the Company's financial statements.

2. SPONSORED RESEARCH AND LICENSE AGREEMENTS

RESEARCH AGREEMENTS

In April 1997, Rigel entered into a two-year sponsored research agreement with Leland Stanford Junior University ("Stanford") for certain patent rights, materials and other know-how relating to the discovery of viral delivery systems. Under the terms of this agreement, Rigel is required to pay research funding fees to be used for salaries and for costs associated with supplies and equipment necessary to perform the research. Stanford retains ownership of all technologies discovered under this agreement, and Rigel has an option to extend the agreement by one year and to acquire all such technologies.

In December 1997, the Company entered into a collaborative agreement with Neurocrine Biosciences, Inc. to discover novel molecular drug targets. The Company granted Neurocrine the right to utilize its technologies in the drug discovery process while Neurocrine granted to the Company the right to utilize various proprietary technologies and compounds. Both companies agreed to fund their own research.

On December 4, 1998, the Company entered into a research collaboration agreement with Janssen Pharmaceutica NV ("Janssen") to research and identify novel targets for drug discovery. Under the terms of the contract, Janssen paid an one time fee and will provide support for research activities during the three-year research period, as well as various milestones and royalties. As part of this collaborative research agreement, Johnson & Johnson ("J&J"), a related company to Janssen, participated in the Company's Series D and E preferred stock financings. J&J contributed $3,000,000 for 1,500,000 shares of Series D preferred stock and contributed $1,000,000 for 166,666 shares of Series E preferred stock.

On January 31, 1999, the Company entered into a two-year collaborative research agreement with Pfizer Inc. to discover and develop various molecular targets. Upon signing of the agreement, Pfizer was

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

2. SPONSORED RESEARCH AND LICENSE AGREEMENTS (CONTINUED)
obligated to pay a one-time, nonrefundable, noncreditable fee. Under the terms of the contract, Pfizer will provide support for research for two years, as well as payment for various milestones and royalty if certain conditions are met. In conjunction with the agreement, Pfizer contributed an additional $2,000,000 in exchange for 1,000,000 shares of Series D preferred stock.

On May 28, 1999, the Company entered into a broad collaboration with Novartis Pharma AG, whereby the Company and Novartis agreed to work on five different research programs to identify various targets for drug development. Two of the five programs were initiated in 1999, with the third program initiated on January 1, 2000. The remaining two programs will be initiated no later than May 28, 2001. Upon the initiation of each research program, Novartis is obligated to pay a one-time, non-refundable, noncreditable fee. For each of the first two programs, Novartis will provide support for research activities for a period of five years. For all programs, Novartis will provide payment for various milestones and royalties if certain conditions, as denoted in the collaboration agreement, are met. In conjunction with the agreement, Novartis contributed an additional $4,000,000 in exchange for 2,000,000 shares of Series D preferred stock. The agreement also allows for an additional equity investment of up to $10,000,000 which is callable by the Company up through an IPO. The price of this additional equity investment is to be determined by the most recent private financing price or IPO price.

In September 1999, the Company entered into a collaborative research and technology agreement with Cell Genesys, Inc. Cell Genesys granted the Company rights to some of its patents and technology. In exchange the Company granted Cell Genesys right to utilize the Company's technology to discover targets in certain therapeutic areas. Both companies will fund their own research.

LICENSE AGREEMENTS

In October 1996, Rigel entered into a license agreement with Stanford for certain patent rights and other know-how relating to the use of retrovirally produced peptide and protein libraries. Under the terms of this agreement, Rigel is required to pay a nonrefundable license fee, minimum royalties and to issue Stanford 65,000 shares of Series A preferred stock. The agreement terminates at the earlier of 20 years or 10 years after the date of the first commercial sale.

In August 1997, Rigel signed a three-year agreement relating to the 1996 agreement to provide the Company with exclusivity to these patents. Under this agreement, Rigel is required to pay a nonrefundable fee and an exclusivity fee over the next three years and issued Stanford 150,000 shares of Series C preferred stock.

At December 31, 1999, the Company's aggregate minimum commitment under all its research and license agreements is approximately $3.1 million. The minimum commitment is $0.4 million in 2000, $0.3 million in 2001, $0.3 million in 2002, $0.3 million in 2003, $0.3 million in 2004, and $1.5 million thereafter.

3. SIGNIFICANT CONCENTRATIONS

In 1998, Janssen represented 100% of total revenues. For the year ended December 31, 1999, Pfizer, Janssen and Novartis accounted for 34%, 32% and 34%, respectively. For the six months ended June 30, 1999, Pfizer, Janssen and Novartis accounted for 45%, 46% and 8%, respectively. For the six months ended June 30, 2000, Pfizer, Janssen and Novartis accounted for 25%, 21% and 53%, respectively. Accounts

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

3. SIGNIFICANT CONCENTRATIONS (CONTINUED)
receivable relate mainly to these three collaborative partners. The Company does not require collateral or other security for accounts receivable.

4. PROPERTY AND EQUIPMENT

Property and equipment consists of the following (in thousands):

<TABLE>
<CAPTION>

	YEARS ENDED DECEMBER 31,	
	1998	1999
<S>	<C>	<C>
Laboratory and office equipment	$ 4,010	$ 8,589
Leasehold improvements	720	2,993
	4,730	11,582
Less accumulated depreciation and amortization	(1,512)	(3,184)
Property and equipment, net	$ 3,218	$ 8,398

</TABLE>

At December 31, 1998 and 1999 equipment under capital leases was approximately $3,317,000 and $9,936,000, respectively with accumulated amortization of approximately $957,000 and $2,736,000, respectively.

5. LONG-TERM OBLIGATIONS

At December 31, 1999 future minimum lease payments under all noncancelable leases are as follows (in thousands):

<TABLE>
<CAPTION>

	CAPITAL LEASES	OPERATING LEASES
<S>	<C>	<C>
2000	$ 2,901	$ 1,463
2001	2,632	2,018
2002	2,161	2,263
2003	1,501	2,333
2004	--	2,353
2005 and thereafter	--	23,035
Total minimum payment required	9,195	$33,465
Less amount representing interest	(1,541)	

Present value of future lease payments	7,654
Less current portion	(2,176)
Noncurrent obligations under capital leases	$ 5,478

</TABLE>

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

5. LONG-TERM OBLIGATIONS (CONTINUED)

The Company leases its South San Francisco office and research facility under a noncancelable operating lease which expires in February 2016. Rent expense under all operating leases amounted to approximately $385,000, $381,000, $1,756,000 for the years ended December 31, 1997, 1998 and 1999 and $1,104,000 for the six months ended June 30, 2000, respectively.

In 1997, the Company entered into an equipment lease line agreement for up to $2,000,000 which was fully utilized in 1998. In June 1998, the Company entered into a second equipment lease line agreement for up to $3,000,000, which was fully utilized in June 1999.

In June 1999 and August 1999, the Company entered into two additional equipment lease line agreements for an aggregate total of $6,000,000, or $3,000,000 each. These lines were fully utilized in May 2000.

The lease periods for all equipment leases are for four years. The interest on each lease is fixed at the time of the draw down with the interest rates ranging from 7% to 15%. Obligations under all leases are secured by the assets financed under the leases.

6. STOCKHOLDERS' EQUITY

In February 2000, the Company completed a private placement of 2,508,330 shares of Series E preferred stock at $6.00 per share for net proceeds of approximately $15.1 million. In addition, the Company issued 50,000 shares of Series E preferred stock for a license of technology. The Company valued the license at $300,000 and has expensed this amount in the six months ended June 30, 2000.

All series of preferred stock are convertible at the stockholders' option at any time into common stock on a one-for-one basis, subject to adjustment for antidilution, and carry voting rights equivalent to common stock. Conversion is automatic upon the closing of an underwritten public offering with aggregate offering proceeds exceeding $15,000,000 and an offering price of at least $3.50 per share (appropriately adjusted for any stock splits, stock dividends, recapitalization or similar events) or upon agreement of the majority of holders of the outstanding shares.

Holders of Series A, B, C, D, and E convertible preferred stock are entitled to noncumulative dividends of $0.008, $0.064, $0.0912, $0.16, and $0.48 per share, respectively, if and when declared by the board of directors. These dividends are to be paid in advance of any distributions to common stockholders. In addition, dividends are to be paid to Series B, C, D, and E stockholders in advance of Series A stockholders. No dividends have been declared through June 30, 2000.

In the event of a liquidation or winding up of the Company, holders of Series A, B, C, D, and E convertible preferred stock shall have a liquidation preference of $0.10, $0.80, $1.14, $2.00, and $6.00 per share, respectively, together with any declared but unpaid dividends, over holders of common shares. Preference shall be given to Series B, C, D, and E stockholders over Series A stockholders.

Preferred stockholders are entitled to the number of votes they would have upon conversion of their preferred shares into common stock.

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

6. STOCKHOLDERS' EQUITY (CONTINUED)

The authorized, issued and outstanding Series A, B, C, D, and E shares of convertible preferred stock were as follows (in thousands):

<TABLE>
<CAPTION>

	DECEMBER 31, 1998			DECEMBER 31, 1999		
	SHARES AUTHORIZED	SHARES ISSUED AND OUTSTANDING	AGGREGATE LIQUIDATION PREFERENCE	SHARES AUTHORIZED	SHARES ISSUED AND OUTSTANDING	AGGREGATE LIQUIDATION PREFERENCE
<S>	<C>	<C>	<C>	<C>	<C>	<C>
Series A.....	665	665	$ 66	665	665	$ 66
Series B.....	7,675	7,500	6,000	7,675	7,500	6,000
Series C.....	8,000	7,387	8,422	8,000	7,407	8,445
Series D.....	5,660	3,482	6,963	7,000	6,482	12,964
Series E.....	--	--	--	--	--	--
Undesignated.....	--	--	--	660	--	--
	22,000	19,034	$21,451	24,000	22,054	$27,475

<CAPTION>

	JUNE 30, 2000 (UNAUDITED)		
	SHARES AUTHORIZED	SHARES ISSUED AND OUTSTANDING	AGGREGATE LIQUIDATION PREFERENCE
<S>	<C>	<C>	<C>
Series A.....	665	665	$ 66
Series B.....	7,675	7,500	6,000
Series C.....	8,000	7,407	8,445
Series D.....	7,000	6,589	13,178
Series E.....	2,750	2,558	15,348
Undesignated.....	660	--	--
	26,750	24,719	$43,037

</TABLE>

WARRANTS

In conjunction with the equipment lease line executed in April 1997, the Company issued a warrant to purchase 175,000 shares of Series B preferred stock at an exercise price of $0.80 per share. The warrant automatically converts upon the earlier of April 30, 2004 or a merger or reorganization of the Company. The fair value of this warrant, as determined using the Black-Scholes valuation model, was approximately $47,000. The amount was expensed in 1997.

In conjunction with the equipment lease line executed in June 1998, the company issued a warrant to purchase 131,578 shares of Series C preferred stock at an exercise price of $1.14 per share. The warrant expires on June 30, 2005. The fair value assigned to this warrant, as determined using the Black-Scholes valuation model, was approximately $86,000. The amount was expensed in 1998.

In conjunction with the Series D preferred stock financing in December 1998, the Company issued five warrants to purchase 191,100 shares of Series D preferred stock at an exercise price of $2.00 per share. These warrants expire at the earlier of the closing of an IPO or December 2003. The fair value assigned to these warrants, as determined using the Black-Scholes valuation model, was approximately $185,000. The amount was expensed in 1998. As of December 31, 1999, warrants to purchase 190,920 shares of Series D preferred stock were outstanding. As of June 30, 2000 warrants to purchase 83,460 shares of Series D preferred stock are outstanding.

In conjunction with the facilities lease entered into in June 1998, the Company issued three warrants to purchase 150,000 shares of common stock at an exercise price of $1.14 per share. The warrants are exercisable at any time up to the earlier of June 1, 2008 or the seventh anniversary of the closing of an initial public offering. The fair value of these warrants was deemed to be immaterial and is not recorded in the financial statements.

2000 STOCK OPTION PLAN

In January 2000, the Company adopted the 2000 Equity Incentive Plan (the "2000 Plan"), which was approved in March 2000 by stockholders. The 2000 Equity Incentive Plan is an amendment and restatement of the 1997 Stock Option Plan. Under the 2000 Plan incentive stock options, nonstatutory

stock options and shares of common stock may be granted to employees, directors of, or consultants to, the Company and its affiliates.

Options granted under the Stock Plan expire no later than 10 years from the date of grant. The option price of each incentive stock option shall be at least 100% of the fair value on the date of grant, and the option price for each nonstatutory stock option shall be not less than 85% of the fair value on the date of grant, as determined by the board of directors. Options may be granted with different vesting terms from time to time but not to exceed five years from the date of grant.

As of June 30, 2000, a total of 9,525,000 shares of common stock have been authorized for issuance under the 2000 Plan.

Activity under the 2000 Plan through June 30, 2000 is as follows:

<TABLE>
<CAPTION>

	SHARES AVAILABLE FOR GRANT	NUMBER OF OPTIONS	WEIGHTED-AVERAGE EXERCISE PRICE
<S>	<C>	<C>	<C>
Outstanding at December 31, 1996	--		
Beginning authorized for grant	2,325,000	--	
Granted	(1,545,000)	1,545,000	$0.10
Exercised	--	(46,667)	0.10
Cancelled	23,333	(23,333)	0.10
Outstanding at December 31, 1997	803,333	1,475,000	0.10
Authorized for grant	3,000,000	--	
Granted	(2,157,500)	2,157,500	0.16
Exercised	--	(118,666)	0.10
Cancelled	159,584	(159,584)	0.12
Outstanding at December 31, 1998	1,805,417	3,354,250	0.14
Authorized for grant	4,200,000	--	
Granted	(2,783,000)	2,783,000	0.24
Exercised	--	(423,001)	0.25
Cancelled	472,245	(472,245)	0.16
Outstanding at December 31, 1999	3,694,662	5,242,004	0.19
Shares granted out of the Plan (unaudited)	(100,000)	--	
Granted (unaudited)	(1,448,599)	1,448,599	5.96
Exercised (unaudited)	--	(1,232,718)	0.16
Cancelled (unaudited)	299,001	(299,001)	4.30
Options outstanding at June 30, 2000 (unaudited)	2,445,064	5,158,884	$1.58

</TABLE>

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

6. STOCKHOLDERS' EQUITY (CONTINUED)

Details of the Company's stock options by exercise price is as follows:

<TABLE>
<CAPTION>

DECEMBER 31, 1999

OPTIONS OUTSTANDING				OPTIONS EXERCISABLE	
EXERCISE PRICE	NUMBER OF OUTSTANDING OPTIONS	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE	WEIGHTED-AVERAGE EXERCISE PRICE	NUMBER OF OPTIONS	WEIGHTED-AVERAGE EXERCISE PRICE
<S>	<C>	<C>	<C>	<C>	<C>
$0.10-$0.30	5,242,004	8.84	$0.19	1,233,294	$0.15
$0.10-$0.30	5,242,004	8.84	$0.19	1,233,294	$0.15

</TABLE>

<TABLE>
<CAPTION>

JUNE 30, 2000 (UNAUDITED)

OPTIONS OUTSTANDING				OPTIONS EXERCISABLE	
EXERCISE PRICE	NUMBER OF OUTSTANDING OPTIONS	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE	WEIGHTED-AVERAGE EXERCISE PRICE	NUMBER OF OPTIONS	WEIGHTED-AVERAGE EXERCISE PRICE

<S>	<C>	<C>	<C>	<C>	<C>	
$0.10 - $ 0.30	3,915,157	8.52	$0.20	731,793	$ 0.19	
$4.50 - $ 7.65	967,075	9.59	$4.84	80,390	$ 4.50	
$9.00 - $11.00	276,652	9.70	$9.64	6,041	$10.09	
$0.10 - $11.00	5,158,884	8.78	$1.58	818,224	$ 0.69	

</TABLE>

The weighted-average fair value of the options granted in 1997, 1998, 1999, and the six months ended June 30, 2000, was $0.02, $0.03, $0.06 and $3.03, respectively.

Pro forma information regarding net loss and net loss per share is required by SFAS 123 and has been determined as if the Company had accounted for its employee stock options under the fair value method prescribed by the Statement. The fair value for these options was estimated at the date of grant using the minimum value method with the following weighted-average assumptions for the years ended December 31, 1997, 1998, 1999 and the six months ended June 30, 2000: risk-free interest rates of 4.5%, 5.5%, 6.0% and 6.0%, respectively; an expected option life of five years; and no dividend yield.

For purposes of pro forma disclosures, the estimated fair value of the options is amortized to expense over the vesting period of the options. The Company's pro forma information follows (in thousands, except per share amounts):

<TABLE>
<CAPTION>

	YEARS ENDED DECEMBER 31,			SIX MONTHS ENDED JUNE 30,
	1997	1998	1999	2000
				(UNAUDITED)
<S>	<C>	<C>	<C>	<C>
Net loss:				
As reported	$(5,516)	$(10,604)	$(12,366)	$(10,801)
Pro forma	(5,516)	(10,604)	(12,413)	(11,692)
Basic and diluted net loss per share:				
As reported	$ (2.20)	$ (4.01)	$ (4.39)	$ (2.60)
Pro forma	(2.20)	(4.01)	(4.40)	(2.81)

</TABLE>

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

6. STOCKHOLDERS' EQUITY (CONTINUED)

The effects of applying SFAS 123 for pro forma disclosures are not likely to be representative of the effects as reported net loss for future years.

The Company granted 621,500 and 334,000 common stock options to consultants in exchange for services in 1998 and 1999, respectively and 130,000 in the six months ended June 30, 2000. The Company has recorded compensation expense related to these options. In accordance with SFAS 123 and EITF 96-18, options granted to consultants are periodically revalued as they vest. On January 27, 2000, the Company granted a total of 100,000 shares of common stock to two individuals for consulting services performed in 1999. The Company has recorded compensation expense related to these grants in 1999.

The Company has recorded deferred stock compensation with respect to options granted to employees of approximately $7.1 million in the year ended December 31, 1999 and $1.5 million for the six months ended June 30, 2000, representing the difference between the exercise price of the options and the deemed fair value of the common stock. These amounts are being amortized to operations over the vesting periods of the options using the graded vesting method. Such amortization expense amounted to approximately $1.3 million for the year ended December 31, 1999 and approximately $2.0 million for the six months ended in June 30, 2000 and is expected to be approximately $1.6 million for the remainder of 2000; $2.0 million in 2001, $1.1 million in 2002, $0.5 million in 2003 and $0.1 million in 2004.

RESERVED SHARES

As of December 31, 1999, the Company has reserved shares of common stock for future issuance as follows:

<TABLE>
<CAPTION>

	DECEMBER 31, 1999

<S>	<C>
Warrants	150,000
Incentive stock plan	8,936,666
Convertible preferred stock	22,551,385
	31,638,051

</TABLE>

In addition, the Company has reserved the following preferred stock for future issuance upon exercise of warrants:

<TABLE>
<CAPTION>

	DECEMBER 31, 1999
<S>	<C>
Series B	175,000
Series C	131,578
Series D	190,920

</TABLE>

7. INCOME TAXES

As of December 31, 1999, the Company had federal and state net operating loss carryforwards of approximately $23.6 million and $4.1 million, respectively. The Company also had federal and California research and development tax credit carryforwards of approximately $700,000 and $500,000. The federal net operating loss and credit carryforwards will expire at various dates beginning in the year 2011 through 2019, if not utilized. The state of California net operating losses will expire beginning in 2005 if not utilized.

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(INFORMATION FOR THE SIX MONTHS ENDED JUNE 30, 2000 IS UNAUDITED)

7. INCOME TAXES (CONTINUED)

Utilization of the federal and state net operating loss and credit carryforwards may be subject to a substantial annual limitation due to the "change in ownership" provisions of the Internal Revenue Code of 1986 (IRC). The annual limitation may result in the expiration of net operating losses and credits before utilization. As of December 31, 1999, an IRC section 382 analysis has not been undertaken to determine the effects of the limitation.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets for financial reporting and the amount used for income tax purposes. Significant components of the Company's deferred tax assets for federal and state income taxes as of December 31 are as follows (in thousands):

<TABLE>
<CAPTION>

	1998	1999
<S>	<C>	<C>
Deferred tax assets		
Net operating loss carryforwards	$ 5,100	$ 8,300
Research and development credits	400	1,000
Capitalized research and development expenses	700	1,100
Other, net	200	400
Total deferred tax assets	6,400	10,800
Valuation allowance	(6,400)	(10,800)
Net deferred taxes	$ --	$ --

</TABLE>

Due to the Company's lack of earnings history, the net deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $2.5 million, $3.9 million and $4.4 million during the years ended December 31, 1997, 1998 and 1999, respectively.

8. SUBSEQUENT EVENTS (UNAUDITED)

INITIAL PUBLIC OFFERING

In August 2000, the board of directors authorized the filing of a registration statement with the Securities and Exchange Commission to register shares of its common stock in connection with a proposed Initial Public Offering. If the offering contemplated by this prospectus is consummated, the

preferred stock outstanding as of the closing date will automatically be converted into shares of the Company's common stock.

In addition, at the closing of the Initial Public Offering, the Company expects to exercise its put option to Novartis Pharma AG for the sale of $10 million of common stock.

ADDITIONAL DEFERRED STOCK COMPENSATION

From July 1, 2000 through August 31, 2000, options to purchase 702,010 shares of the Company's common stock were granted to employees pursuant to the 2000 Equity Incentive Plan with a weighted average exercise price of $5.53. Of these grants, options to purchase 175,000 shares were granted to new hires who will commence employment with the Company at a later date. The deferred stock compensation with respect to these options will be recorded based on the fair value of the Company's common stock at the date employment commences and amortized in accordance with the Company's policy. The Company

8. SUBSEQUENT EVENTS (UNAUDITED) (CONTINUED)

estimates that additional deferred compensation of approximately $1.2 million will be recorded for the remaining 527,010 options granted to employees and amortized in accordance with the Company's policy. Incremental compensation expense from these grants are expected to be approximately $0.3 million in 2000, $0.5 million in 2001, $0.3 million in 2002 and $0.1 million in 2003.

In addition, in the same period, the Company granted options to purchase 20,000 shares of common stock to consultants. Compensation expense related to these options will be recorded in accordance with SFAS 123 and EITF 96-18 as they vest.

2000 EMPLOYEE STOCK PURCHASE PLAN

In August 2000, the Company adopted its 2000 Employee Stock Purchase Plan (the "Purchase Plan") which was approved in September 2000 by shareholders. A total of 400,000 shares of the Company's common stock have been reserved for issuance under the Purchase Plan. In addition, the Purchase Plan provides for annual increases in the number of shares available for issuance under the Purchase Plan on each anniversary date of the effective date of the offering. The number of shares reserved automatically is equal to the lesser of 400,000 shares, 1% of the outstanding shares on the date of the annual increase or such amount as may be determined by the board. The Purchase plan permits eligible employees to purchase common stock at a discount through payroll deductions during defined offering periods. The price at which the stock is purchased is equal to the lower of 85% of the fair market value of the common stock on the first day of the offering or 85% of the fair market value of the Company's common stock on the purchase date. The initial offering period will commence on the effective date of the offering.

2000 NON-EMPLOYEE DIRECTORS' STOCK OPTION PLAN

In August 2000, the Company adopted the 2000 Non-Employee Directors Stock Option Plan, which was approved in September 2000 by stockholders, with a total of 300,000 shares of common stock for issuance thereunder. Each non-employee director who becomes a director of the Company will be automatically granted a nonstatutory stock option to purchase 20,000 shares of common stock on the date on which such person first becomes a director. At each board meeting immediately following each annual stockholders meeting, beginning with the first board meeting after the 2001 Annual Stockholders Meeting, each non-employee director will automatically be granted a nonstatutory option to purchase 5,000 shares of common stock. The exercise price of options under the Directors' Plan will be equal to the fair market value of the common stock on the date of grant. The maximum term of the options granted under the Directors' Plan is ten years. All grants under the Directors' Plan will vest monthly over two years from date of grant. The Directors' Plan will terminate in September 2009, unless terminated earlier in accordance with the provisions of the Directors' Plan.

EQUIPMENT LEASE LINE

In August 2000, the Company entered into an additional equipment lease line agreement for an aggregate total of $5,000,000. The interest is fixed at the time of each draw down. Obligations under this lease will be secured by the assets financed under the lease. At August 31, 2000, the Company has utilized $1.1 million of this lease, for which the interest was fixed at approximately 11%.

[LOGO]

ITEM 13. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The following table sets forth the costs and expenses, other than the underwriting discounts payable by us, in connection with the sale of common stock being registered. All amounts are estimates except the SEC registration fee, the NASD filing fee and the Nasdaq National Market listing fee.

<TABLE>
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SEC registration fee	$ 30,000
NASD filing fee	11,000
Nasdaq National Market listing fee	91,000
Blue sky fees and expenses	25,000
Transfer agent and registrar fees	3,500
Accounting fees and expenses	250,000
Legal fees and expenses	350,000
Printing and engraving costs	200,000
Miscellaneous expenses	39,500
Total	$1,000,000

</TABLE>

ITEM 14. INDEMNIFICATION OF DIRECTORS AND OFFICERS

As permitted by Delaware law, our amended and restated certificate of incorporation provides that no director of ours will be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director, except for liability:

- for any breach of duty of loyalty to us or to our stockholders;

- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;

- for unlawful payment of dividends or unlawful stock repurchases or redemptions under Section 174 of the Delaware General Corporation Law; or

- for any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation further provides that we must indemnify our directors and executive officers and may indemnify our other officers and employees and agents to the fullest extent permitted by Delaware law. We believe that indemnification under our amended and restated certificate of incorporation covers negligence and gross negligence on the part of indemnified parties.

We have entered into indemnification agreements with each of our directors and certain officers. These agreements, among other things, require us to indemnify each director and officer for certain expenses including attorneys' fees, judgments, fines and settlement amounts incurred by any such person in any action or proceeding, including any action by or in the right of Rigel, arising out of the person's services as our director or officer, any subsidiary of ours or any other company or enterprise to which the person provides services at our request.

The underwriting agreement (Exhibit 1.1) will provide for indemnification by the underwriters of Rigel, our directors, our officers who sign the registration statement, and our controlling persons for some liabilities, including liabilities arising under the Securities Act.

ITEM 15. RECENT SALES OF UNREGISTERED SECURITIES

Since July 15, 1996, Rigel has sold and issued unregistered securities to a limited number of persons, as described below. None of these transactions involved any underwriters, underwriting discounts or commissions, or any public offering, and Rigel believes that each transaction was exempt from the

registration requirements of the Securities Act by virtue of Section 4(2) thereof, Regulation D promulgated thereunder or Rule 701 pursuant to compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of securities in each such transaction represented their intention to acquire the securities for investment only and not with a view to or for sale in connection with any distribution thereof, and appropriate legends were affixed to the share certificates and instruments issued in such transactions. We believe that all recipients had adequate access to information about Rigel, through their relationships with Rigel.

Since July 15, 1996, Rigel has sold and issued the following unregistered securities:

(1) From July 15, 1996 to August 31, 2000, we granted incentive stock options

and nonstatutory stock options to purchase an aggregate of 8,656,109 shares of Rigel's common stock at exercise prices ranging from $.10 to $11.00 per share and an aggregate of 100,000 stock awards to employees, directors and consultants under the Plan. Of these stock options 969,830 shares have been canceled without being exercised, 2,063,909 shares have been exercised, 2,500 shares have been repurchased and 5,622,370 shares remain outstanding.

(2) In July 1996 and January 1997, we sold an aggregate of 2,860,000 shares of our common stock to five purchasers at a purchase price of $.001 per share, 350,000 shares of which we repurchased.

(3) From July 1996 to January 1997, we sold an aggregate of 665,000 shares of our Series A preferred stock to four purchasers at a purchase price of $.10 per share.

(4) In January 1997, we sold an aggregate of 7,500,000 shares of our Series B preferred stock to nine purchasers at a purchase price of $.80 per share.

(5) In May 1997, we issued a warrant to purchase 175,000 shares of our Series B preferred stock at a purchase price of $.80 per share.

(6) From November 1997 to January 1998, we sold an aggregate of 7,386,843 shares of our Series C preferred stock to twelve purchasers at a purchase price of $1.14 per share.

(7) On March 27, 1998, we issued 20,000 shares of our Series C preferred stock to one entity for a license for technology.

(8) In June 1998, we issued a warrant to purchase 131,578 shares of our Series C preferred stock at an exercise price of $1.14 per share.

(9) From December 1998 to May 1999, we sold an aggregate of 6,481,864 shares of our Series D preferred stock to ten purchasers at a purchase price of $2.00 per share.

(10) In December 1998, we issued five warrants to purchase an aggregate of 191,100 shares of Series D preferred stock at an exercise price of $2.00 per share, of which 180 shares have been exercised.

(11) On February 3, 2000, we sold an aggregate of 2,508,330 shares of our Series E preferred stock to thirteen purchasers at a purchase price of $6.00 per share, and issued 50,000 shares of Series E preferred stock to one entity for a license for technology.

(12) On August 31, 2000, we sold 33,333 shares of our Series E preferred stock to Thomas S. Volpe, one of our directors, at a purchase price of $6.00 per share.

ITEM 16. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

<TABLE>
<C> <S>
1.1* Form of Underwriting Agreement.
3.1 Amended and Restated Certificate of Incorporation of Rigel to be filed upon the closing of the offering made pursuant to this Registration Statement.
3.2 Amended and Restated Bylaws of Rigel to be adopted upon the closing of the offering made pursuant to this Registration Statement.
</TABLE>

<TABLE>
<C> <S>
4.1 Specimen Common Stock Certificate.
4.2 Amended and Restated Investor Rights Agreement, dated February 3, 2000, between Rigel and holders of Rigel's Series B, Series C, Series D and Series E preferred stock.
4.3 Form of warrant to purchase shares of common stock.
4.4 Warrant issued to Lighthouse Capital Partners II, L.P. for purchase of shares of Series B preferred stock.
4.5 Warrant issued to Lighthouse Capital Partners II, L.P. for purchase of shares of Series C preferred stock.
4.6 Form of warrant to purchase shares of Series D preferred stock.
5.1* Opinion of Cooley Godward LLP.
10.1 Form of Indemnity Agreement.
10.2 2000 Equity Incentive Plan.
10.3 Form of Stock Option Agreement pursuant to 2000 Equity Incentive Plan.
10.4 2000 Employee Stock Purchase Plan.
10.5 2000 Non-Employee Directors' Stock Option Plan.
10.6 Collaboration Agreement between Rigel and Janssen Pharmaceutica N.V., dated December 4, 1998.
10.7 Collaborative Research and License Agreement between Rigel

<TABLE>
	and Pfizer Inc., dated January 31, 1999.
10.8	Collaboration Agreement between Rigel and Novartis Pharma AG, dated May 26, 1999.
10.9++	License and Research Agreement between Rigel and Cell Genesys, Inc., dated September 2, 1999.
10.10	Collaborative Research and Development Agreement between Rigel and Neurocrine Biosciences, Inc., dated December 1997.
10.11	Employment agreement between Rigel and Donald Payan, dated January 16, 1997.
10.12	Lease between Rigel and Britannia Pointe Grand Limited Partnership, dated June 2, 1998.
23.1	Consent of Ernst & Young LLP, Independent Auditors.
23.2	Consent of Cooley Godward LLP (included in Exhibit 5.1).
24.1	Power of Attorney (contained on the signature page).
27.1	Financial Data Schedule.
</TABLE>

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* To be filed by amendment.

++ Confidential treatment requested as to specific portions, which portions are omitted and filed separately with the Securities and Exchange Commission.

ITEM 17. UNDERTAKINGS

The registrant hereby undertakes to provide to the Underwriters at the closing specified in the Underwriting Agreement certificates in such denominations and registered in such names as required by the Underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification by the registrant for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the provisions referenced in Item 14 of this Registration Statement or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act, and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer, or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered hereunder, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether

such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act, the information omitted from the form of Prospectus filed as part of this Registration Statement in reliance upon Rule 430A and contained in a form of Prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this Registration Statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of Prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on the 15th day of September, 2000.

<TABLE>
<S> <C> <C>

RIGEL PHARMACEUTICALS, INC.

By: /s/ JAMES M. GOWER

James M. Gower
CHIEF EXECUTIVE OFFICER
</TABLE>

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below hereby constitutes and appoints James M. Gower and Brian C. Cunningham, and each of them, his or her true and lawful agent, proxy and attorney-in-fact, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to (i) act on, sign and file with the Securities and Exchange Commission any and all amendments (including post-effective amendments) to this registration statement together with all schedules and exhibits thereto and any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended, together with all schedules and exhibits thereto, (ii) act on, sign and file such certificates, instruments, agreements and other documents as may be necessary or appropriate in connection therewith, (iii) act on and file any supplement to any prospectus included in this registration statement or any such amendment or any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended and (iv) take any and all actions which may be necessary or appropriate to be done, as fully for all intents and purposes as he or she might or could do in person, hereby approving, ratifying and confirming all that such agent, proxy and attorney-in-fact or any of his substitutes may lawfully do or cause to be done by virtue thereof.

<TABLE>
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SIGNATURE	TITLE	DATE
<S>	<C>	<C>
/s/ JAMES M. GOWER James M. Gower	President, Chief Executive Officer and Director (PRINCIPAL EXECUTIVE OFFICER)	September 15, 2000
/s/ BRIAN C. CUNNINGHAM Brian C. Cunningham	Senior Vice President, Chief Financial Officer, Chief Operating Officer and Secretary (PRINCIPAL FINANCE AND ACCOUNTING OFFICER)	September 15, 2000
/s/ DONALD G. PAYAN Donald G. Payan	Executive Vice President, Chief Scientific Officer and Director	September 15, 2000
/s/ JEAN DELEAGE Jean Deleage	Director	September 15, 2000
/s/ ALAN D. FRAZIER Alan D. Frazier	Director	September 15, 2000
/s/ WALTER H. MOOS Walter H. Moos	Director	September 15, 2000
/s/ STEPHEN A. SHERWIN Stephen A. Sherwin	Director	September 15, 2000
/s/ THOMAS S. VOLPE Thomas S. Volpe	Director	September 15, 2000

</TABLE>

EXHIBIT INDEX

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* To be filed by amendment.

++ Confidential treatment requested as to specific portions, which portions are omitted and filed separately with the Securities and Exchange Commission.

EXHIBIT A

AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF
RIGEL PHARMACEUTICALS, INC.

I.

The name of this corporation is Rigel Pharmaceuticals, Inc.

II.

The address of the registered office of the corporation in the State of Delaware is 15 East North Street, City of Dover, County of Kent, and the name of the registered agent of the corporation in the State of Delaware at such address is the Incorporating Services, Ltd.

III.

The purpose of this corporation is to engage in any lawful act or activity for which a corporation may be organized under the General Corporation Law of the State of Delaware.

IV.

A. This corporation is authorized to issue two classes of stock to be designated, respectively, "Common Stock" and "Preferred Stock." The total number of shares which the corporation is authorized to issue is one hundred ten million (110,000,000) shares. One hundred million (100,000,000) shares shall be Common Stock, each having a par value of one-tenth of one cent ($.001). Ten million (10,000,000) shares shall be Preferred Stock, each having a par value of one-tenth of one cent ($.001).

B. The Preferred Stock may be issued from time to time in one or more series. The Board of Directors is hereby authorized, by filing a certificate (a "Preferred Stock Designation") pursuant to the Delaware General Corporation Law ("DGCL"), to fix or alter from time to time the designation, powers, preferences and rights of the shares of each such series and the qualifications, limitations or restrictions of any wholly unissued series of Preferred Stock, and to establish from time to time the number of shares constituting any such series or any of them; and to increase or decrease the number of shares of any series subsequent to the issuance of shares of that series, but not below the number of shares of such series then outstanding. In case the number of shares of any series shall be decreased in accordance with the foregoing sentence, the shares constituting such decrease shall resume the status that they had prior to the adoption of the resolution originally fixing the number of shares of such series.

V.

For the management of the business and for the conduct of the affairs of the corporation, and in further definition, limitation and regulation of the powers of the corporation, of its directors and of its stockholders or any class thereof, as the case may be, it is further provided that:

A. NUMBER AND CLASSIFICATION OF DIRECTORS

1. The management of the business and the conduct of the affairs of the corporation shall be vested in its Board of Directors. The number of directors which shall constitute the whole Board of Directors shall be fixed exclusively by one or more resolutions adopted by the Board of Directors.

2. Subject to the rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, following the closing of the initial public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended (the "1933 Act"), covering the offer and sale of Common Stock to the public (the "Initial Public Offering"), the directors shall be divided into three classes designated as Class I, Class II and Class III, respectively. Directors shall be assigned to each class in accordance with a resolution or resolutions adopted by the Board of Directors. At the first annual meeting of stockholders following the closing of the Initial Public Offering, the term of office of the Class I directors shall expire and Class I directors shall be elected for a full term of three years. At the second annual meeting of stockholders following the closing of the Initial Public Offering, the term of office of the Class II directors shall expire and Class II directors shall be elected for a full term of three years.

At the third annual meeting of stockholders following the closing of the Initial Public Offering, the term of office of the Class III directors shall expire and Class III directors shall be elected for a full term of three years. At each succeeding annual meeting of stockholders, directors shall be elected for a full term of three years to succeed the directors of the class whose terms expire at such annual meeting.

Notwithstanding the foregoing provisions of this section, each director shall serve until his successor is duly elected and qualified or until his death, resignation or removal. No decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

3. REMOVAL OF DIRECTORS

a. Neither the Board of Directors nor any individual director may be removed without cause.

b. Subject to any limitation imposed by law, any individual director or directors may be removed with cause by the holders of a majority of the voting power of the corporation entitled to vote at an election of directors.

4. VACANCIES

a. Subject to the rights of the holders of any series of Preferred Stock, any vacancies on the Board of Directors resulting from death, resignation, disqualification, removal or other causes and any newly created directorships resulting from any increase in the number of directors, shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by the stockholders, except as otherwise provided by law, be filled only by the affirmative vote of a majority of the directors then in office, even though less than a quorum of the Board of Directors, and not by the stockholders. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified.

b. If at the time of filling any vacancy or any newly created directorship, the directors then in office shall constitute less than a majority of the whole board (as constituted immediately prior to any such increase), the Delaware Court of Chancery may, upon application of any stockholder or stockholders holding at least ten percent (10%) of the total number of the shares at the time outstanding having the right to vote for such directors, summarily order an election to be held to fill any such vacancies or newly created directorships, or to replace the directors chosen by the directors then in offices as aforesaid, which election shall be governed by Section 211 of the DGCL.

B. BYLAWS AND STOCKHOLDER ACTIONS

1. Subject to paragraph (h) of Section 43 of the Bylaws, the Bylaws may be altered or amended or new Bylaws adopted by the affirmative vote of at least sixty-six and two-thirds percent (66-2/3%) of the voting power of all of the then-outstanding shares of the voting stock of the corporation entitled to vote. The Board of Directors shall also have the power to adopt, amend, or repeal Bylaws.

2. The directors of the corporation need not be elected by written ballot unless the Bylaws so provide.

3. No action shall be taken by the stockholders of the corporation except at an annual or special meeting of stockholders called in accordance with the Bylaws or by written consent of stockholders in accordance with the Bylaws prior to the closing of the Initial Public Offering and following the closing of the Initial Public Offering no action shall be taken by the stockholders by written consent.

4. Advance notice of stockholder nominations for the election of directors and of business to be brought by stockholders before any meeting of the stockholders of the corporation shall be given in the manner provided in the Bylaws of the corporation.

VI.

A. The liability of the directors for monetary damages shall be eliminated to the fullest extent under applicable law.

B. Any repeal or modification of this Article VI shall be prospective and shall not affect the rights under this Article VI in effect at the time of the alleged occurrence of any act or omission to act giving rise to liability or indemnification.

VII.

A. The corporation reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute, except as provided in paragraph B. of this Article VII, and all rights conferred upon the stockholders herein are granted subject to this reservation.

B. Notwithstanding any other provisions of this Certificate of Incorporation or any provision of law which might otherwise permit a lesser vote or no vote, but in addition to any affirmative vote of the holders of any particular class or series of the Voting Stock required by law, this Certificate of Incorporation or any Preferred Stock Designation, the affirmative vote of the holders of at least sixty-six and two-thirds percent (66-2/3%) of the voting power of all of the then-outstanding shares of the voting stock, voting together as a single class, shall be required to alter, amend or repeal Articles.

Exhibit 3.2

AMENDED AND RESTATED BYLAWS

OF

RIGEL PHARMACEUTICALS, INC.
(A DELAWARE CORPORATION)

AMENDED AND RESTATED BYLAWS

OF

RIGEL PHARMACEUTICALS, INC.
(A DELAWARE CORPORATION)

ARTICLE I

OFFICES

SECTION 1. REGISTERED OFFICE. The registered office of the corporation in the State of Delaware shall be in the City of Dover, County of Kent.

SECTION 2. OTHER OFFICES. The corporation shall also have and maintain an office or principal place of business at such place as may be fixed by the Board of Directors, and may also have offices at such other places, both within and without the State of Delaware as the Board of Directors may from time to time determine or the business of the corporation may require.

ARTICLE II

CORPORATE SEAL

SECTION 3. CORPORATE SEAL. The corporate seal shall consist of a die bearing the name of the corporation and the inscription, "Corporate Seal-Delaware." Said seal may be used by causing it or a facsimile thereof to be impressed or affixed or reproduced or otherwise.

ARTICLE III

STOCKHOLDERS' MEETINGS

SECTION 4. PLACE OF MEETINGS. Meetings of the stockholders of the corporation shall be held at such place, either within or without the State of Delaware, as may be designated from time to time by the Board of Directors, or, if not so designated, then at the office of the corporation required to be maintained pursuant to Section 2 hereof.

SECTION 5. ANNUAL MEETINGS.

(a) The annual meeting of the stockholders of the corporation, for the purpose of election of directors and for such other business as may lawfully come before it, shall be held on such date and at such time as may be designated from time to time by the Board of Directors. Nominations of persons for election to the Board of Directors of the corporation and the proposal of business to be considered by the stockholders may be made at an annual meeting of stockholders: (i) pursuant to the corporation's notice of meeting of stockholders; (ii) by or at the direction of the Board of Directors; or (iii) by any stockholder of the corporation who was a stockholder of record at the time of giving of notice provided for in the following paragraph,

who is entitled to vote at the meeting and who complied with the notice procedures set forth in Section 5.

(b) At an annual meeting of the stockholders, only such business shall be conducted as shall have been properly brought before the meeting. For nominations or other business to be properly brought before an annual meeting by a stockholder pursuant to clause (c) of Section 5(a) of these Bylaws, (i) the stockholder must have given timely notice thereof in writing to the Secretary of the corporation, (ii) such other business must be a proper matter for stockholder action under the Delaware General Corporation Law ("DGCL"), (iii) if the stockholder, or the beneficial owner on whose behalf any such proposal or nomination is made, has provided the corporation with a Solicitation Notice (as defined in this Section 5(b)), such stockholder or beneficial owner must, in the case of a proposal, have delivered a proxy statement and form of proxy to holders of at least the percentage of the corporation's voting shares required under applicable law to carry any such proposal, or, in the case of a nomination

or nominations, have delivered a proxy statement and form of proxy to holders of a percentage of the corporation's voting shares reasonably believed by such stockholder or beneficial owner to be sufficient to elect the nominee or nominees proposed to be nominated by such stockholder, and must, in either case, have included in such materials the Solicitation Notice, and (iv) if no Solicitation Notice relating thereto has been timely provided pursuant to this section, the stockholder or beneficial owner proposing such business or nomination must not have solicited a number of proxies sufficient to have required the delivery of such a Solicitation Notice under this Section 5. To be timely, a stockholder's notice shall be delivered to the Secretary at the principal executive offices of the Corporation not later than the close of business on the ninetieth (90th) day nor earlier than the close of business on the one hundred twentieth (120th) day prior to the first anniversary of the preceding year's annual meeting; provided, however, that in the event that the date of the annual meeting is advanced more than thirty (30) days prior to or delayed by more than thirty (30) days after the anniversary of the preceding year's annual meeting, notice by the stockholder to be timely must be so delivered not earlier than the close of business on the one hundred twentieth (120th) day prior to such annual meeting and not later than the close of business on the later of the ninetieth (90th) day prior to such annual meeting or the tenth (10th) day following the day on which public announcement of the date of such meeting is first made. In no event shall the public announcement of an adjournment of an annual meeting commence a new time period for the giving of a stockholder's notice as described above. Such stockholder's notice shall set forth: (A) as to each person whom the stockholder proposed to nominate for election or reelection as a director all information relating to such person that is required to be disclosed in solicitations of proxies for election of directors in an election contest, or is otherwise required, in each case pursuant to Regulation 14A under the Securities Exchange Act of 1934, as amended (the "1934 Act") and Rule 14a-11 thereunder (including such person's written consent to being named in the proxy statement as a nominee and to serving as a director if elected); (B) as to any other business that the stockholder proposes to bring before the meeting, a brief description of the business desired to be brought before the meeting, the reasons for conducting such business at the meeting and any material interest in such business of such stockholder and the beneficial owner, if any, on whose behalf the proposal is made; and (C) as to the stockholder giving the notice and the beneficial owner, if any, on whose behalf the nomination or proposal is made (i) the name and address of such stockholder, as they appear on the corporation's books, and of such beneficial owner, (ii) the class and number of shares of the corporation which are owned beneficially and of record by such stockholder and such beneficial owner, and (iii)

whether either such stockholder or beneficial owner intends to deliver a proxy statement and form of proxy to holders of, in the case of the proposal, at least the percentage of the corporation's voting shares required under applicable law to carry the proposal or, in the case of a nomination or nominations, a sufficient number of holders of the corporation's voting shares to elect such nominee or nominees (an affirmative statement of such intent, a "Solicitation Notice").

(c) Notwithstanding anything in the second sentence of Section 5(b) of these Bylaws to the contrary, in the event that the number of directors to be elected to the Board of Directors of the Corporation is increased and there is no public announcement naming all of the nominees for director or specifying the size of the increased Board of Directors made by the corporation at least one hundred (100) days prior to the first anniversary of the preceding year's annual meeting, a stockholder's notice required by this Section 5 shall also be considered timely, but only with respect to nominees for any new positions created by such increase, if it shall be delivered to the Secretary at the principal executive offices of the corporation not later than the close of business on the tenth (10th) day following the day on which such public announcement is first made by the corporation.

(d) Only such persons who are nominated in accordance with the procedures set forth in this Section 5 shall be eligible to serve as directors and only such business shall be conducted at a meeting of stockholders as shall have been brought before the meeting in accordance with the procedures set forth in this Section 5. Except as otherwise provided by law, the Chairman of the meeting shall have the power and duty to determine whether a nomination or any business proposed to be brought before the meeting was made, or proposed, as the case may be, in accordance with the procedures set forth in these Bylaws and, if any proposed nomination or business is not in compliance with these Bylaws, to declare that such defective proposal or nomination shall not be presented for stockholder action at the meeting and shall be disregarded.

(e) Notwithstanding the foregoing provisions of this Section 5, in order to include information with respect to a stockholder proposal in the proxy statement and form of proxy for a stockholders' meeting, stockholders must provide notice as required by the regulations promulgated under the 1934 Act. Nothing in these Bylaws shall be deemed to affect any rights of stockholders to request inclusion of proposals in the corporation proxy statement pursuant to

Rule 14a-8 under the 1934 Act.

(f) For purposes of this Section 5, "public announcement" shall mean disclosure in a press release reported by the Dow Jones News Service, Associated Press or comparable national news service or in a document publicly filed by the corporation with the Securities and Exchange Commission pursuant to Section 13, 14 or 15(d) of the 1934 Act.

SECTION 6. SPECIAL MEETINGS.

(a) Special meetings of the stockholders of the corporation may be called, for any purpose or purposes, by (i) the Chairman of the Board of Directors, (ii) the Chief Executive Officer, or (iii) the Board of Directors pursuant to a resolution adopted by a majority of the total number of authorized directors (whether or not there exist any vacancies in previously authorized directorships at the time any such resolution is presented to the Board of Directors for adoption).

At any time or times that the corporation is subject to Section 2115(b) of the California General Corporation Law ("CGCL"), stockholders holding five percent (5%) or more of the outstanding shares shall have the right to call a special meeting of stockholders only as set forth in Section 18(c) herein.

(b) If a special meeting is properly called by any person or persons other than the Board of Directors, the request shall be in writing, specifying the general nature of the business proposed to be transacted, and shall be delivered personally or sent by registered mail or by telegraphic or other facsimile transmission to the Chairman of the Board of Directors, the Chief Executive Officer, or the Secretary of the corporation. No business may be transacted at such special meeting otherwise than specified in such notice. The Board of Directors shall determine the time and place of such special meeting, which shall be held not less than thirty-five (35) nor more than one hundred twenty (120) days after the date of the receipt of the request. Upon determination of the time and place of the meeting, the officer receiving the request shall cause notice to be given to the stockholders entitled to vote, in accordance with the provisions of Section 7 of these Bylaws. If the notice is not given within one hundred (100) days after the receipt of the request, the person or persons properly requesting the meeting may set the time and place of the meeting and give the notice. Nothing contained in this paragraph (b) shall be construed as limiting, fixing, or affecting the time when a meeting of stockholders called by action of the Board of Directors may be held.

(c) Nominations of persons for election to the Board of Directors may be made at a special meeting of stockholders at which directors are to be elected pursuant to the corporation's notice of meeting (i) by or at the direction of the Board of Directors or (ii) by any stockholder of the corporation who is a stockholder of record at the time of giving notice provided for in these Bylaws who shall be entitled to vote at the meeting and who complies with the notice procedures set forth in this Section 6(c). In the event the corporation calls a special meeting of stockholders for the purpose of electing one or more directors to the Board of Directors, any such stockholder may nominate a person or persons (as the case may be), for election to such position(s) as specified in the corporation's notice of meeting, if the stockholder's notice required by Section 5(b) of these Bylaws shall be delivered to the Secretary at the principal executive offices of the corporation not earlier than the close of business on the one hundred twentieth (120th) day prior to such special meeting and not later than the close of business on the later of the ninetieth (90th) day prior to such meeting or the tenth (10th) day following the day on which public announcement is first made of the date of the special meeting and of the nominees proposed by the Board of Directors to be elected at such meeting. In no event shall the public announcement of an adjournment of a special meeting commence a new time period for the giving of a stockholder's notice as described above.

SECTION 7. NOTICE OF MEETINGS. Except as otherwise provided by law or the Certificate of Incorporation, written notice of each meeting of stockholders shall be given not less than ten (10) nor more than sixty (60) days before the date of the meeting to each stockholder entitled to vote at such meeting, such notice to specify the place, date and hour and purpose or purposes of the meeting. Notice of the time, place and purpose of any meeting of stockholders may be waived in writing, signed by the person entitled to notice thereof, either before or after such meeting, and will be waived by any stockholder by his attendance thereat in person or by proxy, except when the stockholder attends a meeting for the express purpose of

objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Any stockholder so

waiving notice of such meeting shall be bound by the proceedings of any such meeting in all respects as if due notice thereof had been given.

SECTION 8. QUORUM. At all meetings of stockholders, except where otherwise provided by statute or by the Certificate of Incorporation, or by these Bylaws, the presence, in person or by proxy duly authorized, of the holders of a majority of the outstanding shares of stock entitled to vote shall constitute a quorum for the transaction of business. In the absence of a quorum, any meeting of stockholders may be adjourned, from time to time, either by the chairman of the meeting or by vote of the holders of a majority of the shares represented thereat, but no other business shall be transacted at such meeting. The stockholders present at a duly called or convened meeting, at which a quorum is present, may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum. Except as otherwise provided by statute, the Certificate of Incorporation or these Bylaws, in all matters other than the election of directors, the affirmative vote of the majority of shares present in person or represented by proxy at the meeting and entitled to vote on the subject matter shall be the act of the stockholders. Except as otherwise provided by statute, the Certificate of Incorporation or these Bylaws, directors shall be elected by a plurality of the votes of the shares present in person or represented by proxy at the meeting and entitled to vote on the election of directors. Where a separate vote by a class or classes or series is required, except where otherwise provided by the statute or by the Certificate of Incorporation or these Bylaws, a majority of the outstanding shares of such class or classes or series, present in person or represented by proxy, shall constitute a quorum entitled to take action with respect to that vote on that matter and, except where otherwise provided by the statute or by the Certificate of Incorporation or these Bylaws, the affirmative vote of the majority (plurality, in the case of the election of directors) of the votes cast by the holders of shares of such class or classes or series shall be the act of such class or classes or series.

SECTION 9. ADJOURNMENT AND NOTICE OF ADJOURNED MEETINGS. Any meeting of stockholders, whether annual or special, may be adjourned from time to time either by the chairman of the meeting or by the vote of a majority of the shares casting votes. When a meeting is adjourned to another time or place, notice need not be given of the adjourned meeting if the time and place thereof are announced at the meeting at which the adjournment is taken. At the adjourned meeting, the corporation may transact any business which might have been transacted at the original meeting. If the adjournment is for more than thirty (30) days or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting.

SECTION 10. VOTING RIGHTS. For the purpose of determining those stockholders entitled to vote at any meeting of the stockholders, except as otherwise provided by law, only persons in whose names shares stand on the stock records of the corporation on the record date, as provided in Section 12 of these Bylaws, shall be entitled to vote at any meeting of stockholders. Every person entitled to vote or execute consents shall have the right to do so either in person or by an agent or agents authorized by a proxy granted in accordance with Delaware law. An agent so appointed need not be a stockholder. No proxy shall be voted after three (3) years from its date of creation unless the proxy provides for a longer period.

SECTION 11. JOINT OWNERS OF STOCK. If shares or other securities having voting power stand of record in the names of two (2) or more persons, whether fiduciaries, members of a partnership, joint tenants, tenants in common, tenants by the entirety, or otherwise, or if two (2) or more persons have the same fiduciary relationship respecting the same shares, unless the Secretary is given written notice to the contrary and is furnished with a copy of the instrument or order appointing them or creating the relationship wherein it is so provided, their acts with respect to voting shall have the following effect: (a) if only one (1) votes, his act binds all; (b) if more than one (1) votes, the act of the majority so voting binds all; (c) if more than one (1) votes, but the vote is evenly split on any particular matter, each faction may vote the securities in question proportionally, or may apply to the Delaware Court of Chancery for relief as provided in the DGCL, Section 217(b). If the instrument filed with the Secretary shows that any such tenancy is held in unequal interests, a majority or even-split for the purpose of subsection (c) shall be a majority or even-split in interest.

SECTION 12. LIST OF STOCKHOLDERS. The Secretary shall prepare and make, at least ten (10) days before every meeting of stockholders, a complete list of the stockholders entitled to vote at said meeting, arranged in alphabetical order, showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting, during ordinary business hours, for a period of at least ten (10) days prior to the meeting, either at a place within the city where the meeting is to be held, which place shall be specified in the notice of the meeting, or, if not specified, at the place where

the meeting is to be held. The list shall be produced and kept at the time and place of meeting during the whole time thereof and may be inspected by any stockholder who is present.

SECTION 13. ACTION WITHOUT MEETING.

(a) Unless otherwise provided in the Certificate of Incorporation, any action required by statute to be taken at any annual or special meeting of the stockholders, or any action which may be taken at any annual or special meeting of the stockholders, may be taken without a meeting, without prior notice and without a vote, if a consent in writing, setting forth the action so taken, shall be signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote thereon were present and voted.

(b) Every written consent shall bear the date of signature of each stockholder who signs the consent, and no written consent shall be effective to take the corporate action referred to therein unless, within sixty (60) days of the earliest dated consent delivered to the corporation in the manner herein required, written consents signed by a sufficient number of stockholders to take action are delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to a corporation's registered office shall be by hand or by certified or registered mail, return receipt requested.

(c) Prompt notice of the taking of the corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented

in writing and who, if the action had been taken at a meeting, would have been entitled to notice of the meeting if the record date for such meeting had been the date that written consents signed by a sufficient number of stockholders to take action were delivered to the corporation as provided in Section 228 (c) of the DGCL. If the action which is consented to is such as would have required the filing of a certificate under any section of the DGCL if such action had been voted on by stockholders at a meeting thereof, then the certificate filed under such section shall state, in lieu of any statement required by such section concerning any vote of stockholders, that written consent has been given in accordance with Section 228 of the DGCL.

(d) Notwithstanding the foregoing, no such action by written consent may be taken following the closing of the initial public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended (the "1933 Act"), covering the offer and sale of Common Stock of the corporation (the "Initial Public Offering").

SECTION 14. ORGANIZATION.

(a) At every meeting of stockholders, the Chairman of the Board of Directors, or, if a Chairman has not been appointed or is absent, the President, or, if the President is absent, a chairman of the meeting chosen by a majority in interest of the stockholders entitled to vote, present in person or by proxy, shall act as chairman. The Secretary, or, in his absence, an Assistant Secretary directed to do so by the President, shall act as secretary of the meeting.

(b) The Board of Directors of the corporation shall be entitled to make such rules or regulations for the conduct of meetings of stockholders as it shall deem necessary, appropriate or convenient. Subject to such rules and regulations of the Board of Directors, if any, the chairman of the meeting shall have the right and authority to prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are necessary, appropriate or convenient for the proper conduct of the meeting, including, without limitation, establishing an agenda or order of business for the meeting, rules and procedures for maintaining order at the meeting and the safety of those present, limitations on participation in such meeting to stockholders of record of the corporation and their duly authorized and constituted proxies and such other persons as the chairman shall permit, restrictions on entry to the meeting after the time fixed for the commencement thereof, limitations on the time allotted to questions or comments by participants and regulation of the opening and closing of the polls for balloting on matters which are to be voted on by ballot. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with rules of parliamentary procedure.

ARTICLE IV

DIRECTORS

SECTION 15. NUMBER AND TERM OF OFFICE. The authorized number of directors

of the corporation shall be fixed in accordance with the Certificate of Incorporation. Directors need not be stockholders unless so required by the Certificate of Incorporation. If for any cause, the directors shall not have been elected at an annual meeting, they may be elected as soon thereafter

as convenient at a special meeting of the stockholders called for that purpose in the manner provided in these Bylaws.

SECTION 16. POWERS. The powers of the corporation shall be exercised, its business conducted and its property controlled by the Board of Directors, except as may be otherwise provided by statute or by the Certificate of Incorporation.

SECTION 17. CLASSES OF DIRECTORS. Subject to the rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, following the closing of the Initial Public Offering, the directors shall be divided into three classes designated as Class I, Class II and Class III, respectively. Directors shall be assigned to each class in accordance with a resolution or resolutions adopted by the Board of Directors. At the first annual meeting of stockholders following the closing of the Initial Public Offering, the term of office of the Class I directors shall expire and Class I directors shall be elected for a full term of three years. At the second annual meeting of stockholders following the closing of the Initial Public Offering, the term of office of the Class II directors shall expire and Class II directors shall be elected for a full term of three years. At the third annual meeting of stockholders following the closing of the Initial Public Offering, the term of office of the Class III directors shall expire and Class III directors shall be elected for a full term of three years. At each succeeding annual meeting of stockholders, directors shall be elected for a full term of three years to succeed the directors of the class whose terms expire at such annual meeting.

Notwithstanding the foregoing provisions of this section, each director shall serve until his successor is duly elected and qualified or until his death, resignation or removal. No decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

SECTION 18. VACANCIES.

(a) Unless otherwise provided in the Certificate of Incorporation, any vacancies on the Board of Directors resulting from death, resignation, disqualification, removal or other causes and any newly created directorships resulting from any increase in the number of directors shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by stockholders, be filled only by the affirmative vote of a majority of the directors then in office, even though less than a quorum of the Board of Directors. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified. A vacancy in the Board of Directors shall be deemed to exist under this Section 18 in the case of the death, removal or resignation of any director.

(b) If at the time of filling any vacancy or any newly created directorship, the directors then in office shall constitute less than a majority of the whole board (as constituted immediately prior to any such increase), the Delaware Court of Chancery may, upon application of any stockholder or stockholders holding at least ten percent (10%) of the total number of the shares at the time outstanding having the right to vote for such directors, summarily order an election to be held to fill any such vacancies or newly created directorships, or to replace the

directors chosen by the directors then in offices as aforesaid, which election shall be governed by Section 211 of the DGCL.

SECTION 19. RESIGNATION. Any director may resign at any time by delivering his written resignation to the Secretary, such resignation to specify whether it will be effective at a particular time, upon receipt by the Secretary or at the pleasure of the Board of Directors. If no such specification is made, it shall be deemed effective at the pleasure of the Board of Directors. When one or more directors shall resign from the Board of Directors, effective at a future date, a majority of the directors then in office, including those who have so resigned, shall have power to fill such vacancy or vacancies, the vote thereon to take effect when such resignation or resignations shall become effective, and each Director so chosen shall hold office for the unexpired portion of the term of the Director whose place shall be vacated and until his successor shall have been duly elected and qualified.

SECTION 20. REMOVAL.

(a) Neither the Board of Directors nor any individual director may be removed without cause.

(b) Subject to any limitation imposed by law, any individual director or directors may be removed with cause by the affirmative vote of a majority of the voting power of the corporation entitled to vote at an election of directors.

SECTION 21. MEETINGS.

(a) ANNUAL MEETINGS. The annual meeting of the Board of Directors shall be held immediately before or after the annual meeting of stockholders and at the place where such meeting is held. No notice of an annual meeting of the Board of Directors shall be necessary and such meeting shall be held for the purpose of electing officers and transacting such other business as may lawfully come before it.

(b) REGULAR MEETINGS. Unless otherwise restricted by the Certificate of Incorporation, regular meetings of the Board of Directors may be held at any time or date and at any place within or without the State of Delaware which has been designated by the Board of Directors and publicized among all directors. No formal notice shall be required for regular meetings of the Board of Directors.

(c) SPECIAL MEETINGS. Unless otherwise restricted by the Certificate of Incorporation, special meetings of the Board of Directors may be held at any time and place within or without the State of Delaware whenever called by the Chairman of the Board, the President or any two of the directors.

(d) TELEPHONE MEETINGS. Any member of the Board of Directors, or of any committee thereof, may participate in a meeting by means of conference telephone or similar communications equipment by means of which all persons participating in the meeting can hear each other, and participation in a meeting by such means shall constitute presence in person at such meeting.

(e) NOTICE OF MEETINGS. Notice of the time and place of all special meetings of the Board of Directors shall be orally or in writing, by telephone, including a voice messaging system or other system or technology designed to record and communicate messages, facsimile, telegraph or telex, or by electronic mail or other electronic means, during normal business hours, at least twenty-four (24) hours before the date and time of the meeting, or sent in writing to each director by first class mail, charges prepaid, at least three (3) days before the date of the meeting. Notice of any meeting may be waived in writing at any time before or after the meeting and will be waived by any director by attendance thereat, except when the director attends the meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

(f) WAIVER OF NOTICE. The transaction of all business at any meeting of the Board of Directors, or any committee thereof, however called or noticed, or wherever held, shall be as valid as though had at a meeting duly held after regular call and notice, if a quorum be present and if, either before or after the meeting, each of the directors not present shall sign a written waiver of notice. All such waivers shall be filed with the corporate records or made a part of the minutes of the meeting.

SECTION 22. QUORUM AND VOTING.

(a) Unless the Certificate of Incorporation requires a greater number and except with respect to indemnification questions arising under Section 43 hereof, for which a quorum shall be one-third of the exact number of directors fixed from time to time in accordance with the Certificate of Incorporation, a quorum of the Board of Directors shall consist of a majority of the exact number of directors fixed from time to time by the Board of Directors in accordance with the Certificate of Incorporation; PROVIDED, HOWEVER, at any meeting whether a quorum be present or otherwise, a majority of the directors present may adjourn from time to time until the time fixed for the next regular meeting of the Board of Directors, without notice other than by announcement at the meeting.

(b) At each meeting of the Board of Directors at which a quorum is present, all questions and business shall be determined by the affirmative vote of a majority of the directors present, unless a different vote be required by law, the Certificate of Incorporation or these Bylaws.

SECTION 23. ACTION WITHOUT MEETING. Unless otherwise restricted by the Certificate of Incorporation or these Bylaws, any action required or permitted to be taken at any meeting of the Board of Directors or of any committee thereof

may be taken without a meeting, if all members of the Board of Directors or committee, as the case may be, consent thereto in writing, and such writing or writings are filed with the minutes of proceedings of the Board of Directors or committee.

SECTION 24. FEES AND COMPENSATION. Directors shall be entitled to such compensation for their services as may be approved by the Board of Directors, including, if so approved, by resolution of the Board of Directors, a fixed sum and expenses of attendance, if any, for attendance at each regular or special meeting of the Board of Directors and at any meeting of a committee of the Board of Directors. Nothing herein contained shall be construed

to preclude any director from serving the corporation in any other capacity as an officer, agent, employee, or otherwise and receiving compensation therefor.

SECTION 25. COMMITTEES.

(a) EXECUTIVE COMMITTEE. The Board of Directors may appoint an Executive Committee to consist of one (1) or more members of the Board of Directors. The Executive Committee, to the extent permitted by law and provided in the resolution of the Board of Directors shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation, and may authorize the seal of the corporation to be affixed to all papers which may require it; but no such committee shall have the power or authority in reference to (i) approving or adopting, or recommending to the stockholders, any action or matter expressly required by the DGCL to be submitted to stockholders for approval, or (ii) adopting, amending or repealing any bylaw of the corporation.

(b) OTHER COMMITTEES. The Board of Directors may, from time to time, appoint such other committees as may be permitted by law. Such other committees appointed by the Board of Directors shall consist of one (1) or more members of the Board of Directors and shall have such powers and perform such duties as may be prescribed by the resolution or resolutions creating such committees, but in no event shall any such committee have the powers denied to the Executive Committee in these Bylaws.

(c) TERM. Each member of a committee of the Board of Directors shall serve a term on the committee coexistent with such member's term on the Board of Directors. The Board of Directors, subject to any requirements of any outstanding series of preferred Stock and the provisions of subsections (a) or (b) of this Bylaw, may at any time increase or decrease the number of members of a committee or terminate the existence of a committee. The membership of a committee member shall terminate on the date of his death or voluntary resignation from the committee or from the Board of Directors. The Board of Directors may at any time for any reason remove any individual committee member and the Board of Directors may fill any committee vacancy created by death, resignation, removal or increase in the number of members of the committee. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee, and, in addition, in the absence or disqualification of any member of a committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not he or they constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in the place of any such absent or disqualified member.

(d) MEETINGS. Unless the Board of Directors shall otherwise provide, regular meetings of the Executive Committee or any other committee appointed pursuant to this Section 25 shall be held at such times and places as are determined by the Board of Directors, or by any such committee, and when notice thereof has been given to each member of such committee, no further notice of such regular meetings need be given thereafter. Special meetings of any such committee may be held at any place which has been determined from time to time by such committee, and may be called by any director who is a member of such committee, upon written notice to the members of such committee of the time and place of such special meeting

given in the manner provided for the giving of written notice to members of the Board of Directors of the time and place of special meetings of the Board of Directors. Notice of any special meeting of any committee may be waived in writing at any time before or after the meeting and will be waived by any director by attendance thereat, except when the director attends such special meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. A majority of the authorized number of members of any such committee shall constitute a quorum for the transaction of business, and the act of a majority of those present at any meeting at which a quorum is present shall be

the act of such committee.

SECTION 26. ORGANIZATION. At every meeting of the directors, the Chairman of the Board of Directors, or, if a Chairman has not been appointed or is absent, the President (if a director), or if the President is absent, the most senior Vice President (if a director), or, in the absence of any such person, a chairman of the meeting chosen by a majority of the directors present, shall preside over the meeting. The Secretary, or in his absence, any Assistant Secretary directed to do so by the President, shall act as secretary of the meeting.

ARTICLE V

OFFICERS

SECTION 27. OFFICERS DESIGNATED. The officers of the corporation shall include, if and when designated by the Board of Directors, the Chairman of the Board of Directors, the Chief Executive Officer, the President, one or more Vice Presidents, the Secretary, the Chief Financial Officer, the Treasurer and the Controller, all of whom shall be elected at the annual organizational meeting of the Board of Directors. The Board of Directors may also appoint one or more Assistant Secretaries, Assistant Treasurers, Assistant Controllers and such other officers and agents with such powers and duties as it shall deem necessary. The Board of Directors may assign such additional titles to one or more of the officers as it shall deem appropriate. Any one person may hold any number of offices of the corporation at any one time unless specifically prohibited therefrom by law. The salaries and other compensation of the officers of the corporation shall be fixed by or in the manner designated by the Board of Directors.

SECTION 28. TENURE AND DUTIES OF OFFICERS.

(a) GENERAL. All officers shall hold office at the pleasure of the Board of Directors and until their successors shall have been duly elected and qualified, unless sooner removed. Any officer elected or appointed by the Board of Directors may be removed at any time by the Board of Directors. If the office of any officer becomes vacant for any reason, the vacancy may be filled by the Board of Directors.

(b) DUTIES OF CHAIRMAN OF THE BOARD OF DIRECTORS. The Chairman of the Board of Directors, when present, shall preside at all meetings of the stockholders and the Board of Directors. The Chairman of the Board of Directors shall perform other duties commonly incident to his office and shall also perform such other duties and have such other powers, as the Board of Directors shall designate from time to time. If there is no President, then the Chairman

of the Board of Directors shall also serve as the Chief Executive Officer of the corporation and shall have the powers and duties prescribed in paragraph (c) of this Section 28.

(c) DUTIES OF PRESIDENT. The President shall preside at all meetings of the stockholders and at all meetings of the Board of Directors, unless the Chairman of the Board of Directors has been appointed and is present. Unless some other officer has been elected Chief Executive Officer of the corporation, the President shall be the chief executive officer of the corporation and shall, subject to the control of the Board of Directors, have general supervision, direction and control of the business and officers of the corporation. The President shall perform other duties commonly incident to his office and shall also perform such other duties and have such other powers, as the Board of Directors shall designate from time to time.

(d) DUTIES OF VICE PRESIDENTS. The Vice Presidents may assume and perform the duties of the President in the absence or disability of the President or whenever the office of President is vacant. The Vice Presidents shall perform other duties commonly incident to their office and shall also perform such other duties and have such other powers as the Board of Directors or the President shall designate from time to time.

(e) DUTIES OF SECRETARY. The Secretary shall attend all meetings of the stockholders and of the Board of Directors and shall record all acts and proceedings thereof in the minute book of the corporation. The Secretary shall give notice in conformity with these Bylaws of all meetings of the stockholders and of all meetings of the Board of Directors and any committee thereof requiring notice. The Secretary shall perform all other duties given him in these Bylaws and other duties commonly incident to his office and shall also perform such other duties and have such other powers, as the Board of Directors shall designate from time to time. The President may direct any Assistant Secretary to assume and perform the duties of the Secretary in the absence or disability of the Secretary, and each Assistant Secretary shall perform other duties commonly incident to his office and shall also perform such other duties and have such other powers as the Board of Directors or the President shall

designate from time to time.

(f) DUTIES OF CHIEF FINANCIAL OFFICER. The Chief Financial Officer shall keep or cause to be kept the books of account of the corporation in a thorough and proper manner and shall render statements of the financial affairs of the corporation in such form and as often as required by the Board of Directors or the President. The Chief Financial Officer, subject to the order of the Board of Directors, shall have the custody of all funds and securities of the corporation. The Chief Financial Officer shall perform other duties commonly incident to his office and shall also perform such other duties and have such other powers as the Board of Directors or the President shall designate from time to time. The President may direct the Treasurer or any Assistant Treasurer, or the Controller or any Assistant Controller to assume and perform the duties of the Chief Financial Officer in the absence or disability of the Chief Financial Officer, and each Treasurer and Assistant Treasurer and each Controller and Assistant Controller shall perform other duties commonly incident to his office and shall also perform such other duties and have such other powers as the Board of Directors or the President shall designate from time to time.

SECTION 29. DELEGATION OF AUTHORITY. The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

SECTION 30. RESIGNATIONS. Any officer may resign at any time by giving written notice to the Board of Directors or to the President or to the Secretary. Any such resignation shall be effective when received by the person or persons to whom such notice is given, unless a later time is specified therein, in which event the resignation shall become effective at such later time. Unless otherwise specified in such notice, the acceptance of any such resignation shall not be necessary to make it effective. Any resignation shall be without prejudice to the rights, if any, of the corporation under any contract with the resigning officer.

SECTION 31. REMOVAL. Any officer may be removed from office at any time, either with or without cause, by the affirmative vote of a majority of the directors in office at the time, or by the unanimous written consent of the directors in office at the time, or by any committee or superior officers upon whom such power of removal may have been conferred by the Board of Directors.

ARTICLE VI

EXECUTION OF CORPORATE INSTRUMENTS AND VOTING OF SECURITIES OWNED BY THE CORPORATION

SECTION 32. EXECUTION OF CORPORATE INSTRUMENTS. The Board of Directors may, in its discretion, determine the method and designate the signatory officer or officers, or other person or persons, to execute on behalf of the corporation any corporate instrument or document, or to sign on behalf of the corporation the corporate name without limitation, or to enter into contracts on behalf of the corporation, except where otherwise provided by law or these Bylaws, and such execution or signature shall be binding upon the corporation.

All checks and drafts drawn on banks or other depositaries on funds to the credit of the corporation or in special accounts of the corporation shall be signed by such person or persons as the Board of Directors shall authorize so to do.

Unless authorized or ratified by the Board of Directors or within the agency power of an officer, no officer, agent or employee shall have any power or authority to bind the corporation by any contract or engagement or to pledge its credit or to render it liable for any purpose or for any amount.

SECTION 33. VOTING OF SECURITIES OWNED BY THE CORPORATION. All stock and other securities of other corporations owned or held by the corporation for itself, or for other parties in any capacity, shall be voted, and all proxies with respect thereto shall be executed, by the person authorized so to do by resolution of the Board of Directors, or, in the absence of such authorization, by the Chairman of the Board of Directors, the Chief Executive Officer, the President, or any Vice President.

ARTICLE VII

SHARES OF STOCK

SECTION 34. FORM AND EXECUTION OF CERTIFICATES. Certificates for the shares of stock of the corporation shall be in such form as is consistent with the

Certificate of Incorporation and applicable law. Every holder of stock in the corporation shall be entitled to have a certificate signed by or in the name of the corporation by the Chairman of the Board of Directors, or the President or any Vice President and by the Treasurer or Assistant Treasurer or the Secretary or Assistant Secretary, certifying the number of shares owned by him in the corporation. Any or all of the signatures on the certificate may be facsimiles. In case any officer, transfer agent, or registrar who has signed or whose facsimile signature has been placed upon a certificate shall have ceased to be such officer, transfer agent, or registrar before such certificate is issued, it may be issued with the same effect as if he were such officer, transfer agent, or registrar at the date of issue. Each certificate shall state upon the face or back thereof, in full or in summary, all of the powers, designations, preferences, and rights, and the limitations or restrictions of the shares authorized to be issued or shall, except as otherwise required by law, set forth on the face or back a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative, participating, optional, or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights. Within a reasonable time after the issuance or transfer of uncertificated stock, the corporation shall send to the registered owner thereof a written notice containing the information required to be set forth or stated on certificates pursuant to this section or otherwise required by law or with respect to this section a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights. Except as otherwise expressly provided by law, the rights and obligations of the holders of certificates representing stock of the same class and series shall be identical.

SECTION 35. LOST CERTIFICATES. A new certificate or certificates shall be issued in place of any certificate or certificates theretofore issued by the corporation alleged to have been lost, stolen, or destroyed, upon the making of an affidavit of that fact by the person claiming the certificate of stock to be lost, stolen, or destroyed. The corporation may require, as a condition precedent to the issuance of a new certificate or certificates, the owner of such lost, stolen, or destroyed certificate or certificates, or his legal representative, to agree to indemnify the corporation in such manner as it shall require or to give the corporation a surety bond in such form and amount as it may direct as indemnity against any claim that may be made against the corporation with respect to the certificate alleged to have been lost, stolen, or destroyed.

SECTION 36. TRANSFERS.

(a) Transfers of record of shares of stock of the corporation shall be made only upon its books by the holders thereof, in person or by attorney duly authorized, and upon the surrender of a properly endorsed certificate or certificates for a like number of shares.

(b) The corporation shall have power to enter into and perform any agreement with any number of stockholders of any one or more classes of stock of the corporation to restrict the transfer of shares of stock of the corporation of any one or more classes owned by such stockholders in any manner not prohibited by the DGCL.

SECTION 37. FIXING RECORD DATES.

(a) In order that the corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, the Board of Directors may fix, in advance, a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date shall, subject to applicable law, not be more than sixty (60) nor less than ten (10) days before the date of such meeting. If no record date is fixed by the Board of Directors, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or if notice is waived, at the close of business on the day next preceding the day on which the meeting is held. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; PROVIDED, HOWEVER, that the Board of Directors may fix a new record date for the adjourned meeting.

(b) Prior to the Initial Public Offering in order that the corporation may determine the stockholders entitled to consent to corporate action in writing without a meeting, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which date shall not be more than ten (10) days after the date upon which the resolution fixing the

record date is adopted by the Board of Directors. Any stockholder of record seeking to have the stockholders authorize or take corporate action by written consent shall, by written notice to the Secretary, request the Board of Directors to fix a record date. The Board of Directors shall promptly, but in all events within ten (10) days after the date on which such a request is received, adopt a resolution fixing the record date. If no record date has been fixed by the Board of Directors within ten (10) days of the date on which such a request is received, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting, when no prior action by the Board of Directors is required by applicable law, shall be the first date on which a signed written consent setting forth the action taken or proposed to be taken is delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to the corporation's registered office shall be by hand or by certified or registered mail, return receipt requested. If no record date has been fixed by the Board of Directors and prior action by the Board of Directors is required by law, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting shall be at the close of business on the day on which the Board of Directors adopts the resolution taking such prior action.

(c) In order that the corporation may determine the stockholders entitled to receive payment of any dividend or other distribution or allotment of any rights or the stockholders entitled to exercise any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action, the Board of Directors may fix, in advance, a

record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted, and which record date shall be not more than sixty (60) days prior to such action. If no record date is fixed, the record date for determining stockholders for any such purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto.

SECTION 38. REGISTERED STOCKHOLDERS. The corporation shall be entitled to recognize the exclusive right of a person registered on its books as the owner of shares to receive dividends, and to vote as such owner, and shall not be bound to recognize any equitable or other claim to or interest in such share or shares on the part of any other person whether or not it shall have express or other notice thereof, except as otherwise provided by the laws of Delaware.

ARTICLE VIII

OTHER SECURITIES OF THE CORPORATION

SECTION 39. EXECUTION OF OTHER SECURITIES. All bonds, debentures and other corporate securities of the corporation, other than stock certificates (covered in Section 34), may be signed by the Chairman of the Board of Directors, the President or any Vice President, or such other person as may be authorized by the Board of Directors, and the corporate seal impressed thereon or a facsimile of such seal imprinted thereon and attested by the signature of the Secretary or an Assistant Secretary, or the Chief Financial Officer or Treasurer or an Assistant Treasurer; PROVIDED, HOWEVER, that where any such bond, debenture or other corporate security shall be authenticated by the manual signature, or where permissible facsimile signature, of a trustee under an indenture pursuant to which such bond, debenture or other corporate security shall be issued, the signatures of the persons signing and attesting the corporate seal on such bond, debenture or other corporate security may be the imprinted facsimile of the signatures of such persons. Interest coupons appertaining to any such bond, debenture or other corporate security, authenticated by a trustee as aforesaid, shall be signed by the Treasurer or an Assistant Treasurer of the corporation or such other person as may be authorized by the Board of Directors, or bear imprinted thereon the facsimile signature of such person. In case any officer who shall have signed or attested any bond, debenture or other corporate security, or whose facsimile signature shall appear thereon or on any such interest coupon, shall have ceased to be such officer before the bond, debenture or other corporate security so signed or attested shall have been delivered, such bond, debenture or other corporate security nevertheless may be adopted by the corporation and issued and delivered as though the person who signed the same or whose facsimile signature shall have been used thereon had not ceased to be such officer of the corporation.

ARTICLE IX

DIVIDENDS

SECTION 40. DECLARATION OF DIVIDENDS. Dividends upon the capital stock of the corporation, subject to the provisions of the Certificate of Incorporation and applicable law, if any, may be declared by the Board of Directors pursuant to law at any regular or special meeting.

Dividends may be paid in cash, in property, or in shares of the capital stock, subject to the provisions of the Certificate of Incorporation and applicable law.

SECTION 41. DIVIDEND RESERVE. Before payment of any dividend, there may be set aside out of any funds of the corporation available for dividends such sum or sums as the Board of Directors from time to time, in their absolute discretion, think proper as a reserve or reserves to meet contingencies, or for equalizing dividends, or for repairing or maintaining any property of the corporation, or for such other purpose as the Board of Directors shall think conducive to the interests of the corporation, and the Board of Directors may modify or abolish any such reserve in the manner in which it was created.

ARTICLE X

FISCAL YEAR

SECTION 42. FISCAL YEAR. The fiscal year of the corporation shall be fixed by resolution of the Board of Directors.

ARTICLE XI

INDEMNIFICATION

SECTION 43. INDEMNIFICATION OF DIRECTORS, EXECUTIVE OFFICERS, OTHER OFFICERS, EMPLOYEES AND OTHER AGENTS.

(a) DIRECTORS AND EXECUTIVE OFFICERS. The corporation shall indemnify its directors and executive officers (for the purposes of this Article XI, "executive officers" shall have the meaning defined in Rule 3b-7 promulgated under the 1934 Act) to the fullest extent not prohibited by the DGCL or any other applicable law; PROVIDED, HOWEVER, that the corporation may modify the extent of such indemnification by individual contracts with its directors and executive officers; and, PROVIDED, FURTHER, that the corporation shall not be required to indemnify any director or executive officer in connection with any proceeding (or part thereof) initiated by such person unless (i) such indemnification is expressly required to be made by law, (ii) the proceeding was authorized by the Board of Directors of the corporation, (iii) such indemnification is provided by the corporation, in its sole discretion, pursuant to the powers vested in the corporation under the DGCL or any other applicable law or (iv) such indemnification is required to be made under subsection (d).

(b) OTHER OFFICERS, EMPLOYEES AND OTHER AGENTS. The corporation shall have power to indemnify its other officers, employees and other agents as set forth in the DGCL or any other applicable law. The Board of Directors shall have the power to delegate the determination of whether indemnification shall be given to any such person except executive officers to such officers or other persons as the Board of Directors shall determine.

(c) EXPENSES. The corporation shall advance to any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he is or was a director or executive officer, of the corporation, or is or was serving at the request of

the corporation as a director or executive officer of another corporation, partnership, joint venture, trust or other enterprise, prior to the final disposition of the proceeding, promptly following request therefor, all expenses incurred by any director in connection with such proceeding upon receipt of an undertaking by or on behalf of such person to repay said amounts if it should be determined ultimately that such person is not entitled to be indemnified under this Section 43 or otherwise.

Notwithstanding the foregoing, unless otherwise determined pursuant to paragraph (e) of this Section 43, no advance shall be made by the corporation to an executive officer of the corporation (except by reason of the fact that such executive officer is or was a director of the corporation in which event this paragraph shall not apply) in any action, suit or proceeding, whether civil, criminal, administrative or investigative, if a determination is reasonably and promptly made (i) by the Board of Directors by a majority vote of a quorum consisting of directors who were not parties to the proceeding, or (ii) if such quorum is not obtainable, or, even if obtainable, a quorum of disinterested directors so directs, by independent legal counsel in a written opinion, that the facts known to the decision-making party at the time such determination is made demonstrate clearly and convincingly that such person acted in bad faith or in a manner that such person did not believe to be in or not opposed to the best

interests of the corporation.

(d) ENFORCEMENT. Without the necessity of entering into an express contract, all rights to indemnification and advances to directors and executive officers under this Bylaw shall be deemed to be contractual rights and be effective to the same extent and as if provided for in a contract between the corporation and the director or executive officer Any right to indemnification or advances granted by this Section 43 to a director or executive officer shall be enforceable by or on behalf of the person holding such right in any court of competent jurisdiction if (i) the claim for indemnification or advances is denied, in whole or in part, or (ii) no disposition of such claim is made within ninety (90) days of request therefor. The claimant in such enforcement action, if successful in whole or in part, shall be entitled to be paid also the expense of prosecuting his claim. In connection with any claim for indemnification, the corporation shall be entitled to raise as a defense to any such action that the claimant has not met the standards of conduct that make it permissible under the DGCL or any other applicable law for the corporation to indemnify the claimant for the amount claimed. In connection with any claim by an executive officer of the corporation (except in any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that such executive officer is or was a director of the corporation) for advances, the corporation shall be entitled to raise a defense as to any such action clear and convincing evidence that such person acted in bad faith or in a manner that such person did not believe to be in or not opposed to the best interests of the corporation, or with respect to any criminal action or proceeding that such person acted without reasonable cause to believe that his conduct was lawful. Neither the failure of the corporation (including its Board of Directors, independent legal counsel or its stockholders) to have made a determination prior to the commencement of such action that indemnification of the claimant is proper in the circumstances because he has met the applicable standard of conduct set forth in the DGCL or any other applicable law, nor an actual determination by the corporation (including its Board of Directors, independent legal counsel or its stockholders) that the claimant has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that claimant has not met the applicable standard of conduct. In any suit brought by a director or executive officer to enforce a right to indemnification or to an advancement of

expenses hereunder, the burden of proving that the director or executive officer is not entitled to be indemnified, or to such advancement of expenses, under this Section 43 or otherwise shall be on the corporation.

(e) NON-EXCLUSIVITY OF RIGHTS. The rights conferred on any person by this Bylaw shall not be exclusive of any other right which such person may have or hereafter acquire under any applicable statute, provision of the Certificate of Incorporation, Bylaws, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his official capacity and as to action in another capacity while holding office. The corporation is specifically authorized to enter into individual contracts with any or all of its directors, officers, employees or agents respecting indemnification and advances, to the fullest extent not prohibited by the Delaware General Corporation Law, or by any other applicable law.

(f) SURVIVAL OF RIGHTS. The rights conferred on any person by this Bylaw shall continue as to a person who has ceased to be a director, officer, employee or other agent and shall inure to the benefit of the heirs, executors and administrators of such a person.

(g) INSURANCE. To the fullest extent permitted by the DGCL or any other applicable law, the corporation, upon approval by the Board of Directors, may purchase insurance on behalf of any person required or permitted to be indemnified pursuant to this Section 43.

(h) AMENDMENTS. Any repeal or modification of this Section 43 shall only be prospective and shall not affect the rights under this Bylaw in effect at the time of the alleged occurrence of any action or omission to act that is the cause of any proceeding against any agent of the corporation.

(i) SAVING CLAUSE. If this Bylaw or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the corporation shall nevertheless indemnify each director and executive officer to the full extent not prohibited by any applicable portion of this Section 43 that shall not have been invalidated, or by any other applicable law. If this Section 43 shall be invalid due to the application of the indemnification provisions of another jurisdiction, then the corporation shall indemnify each director and executive officer to the full extent under any other applicable law.

(j) CERTAIN DEFINITIONS. For the purposes of this Bylaw, the following definitions shall apply:

(1) The term "proceeding" shall be broadly construed and shall

include, without limitation, the investigation, preparation, prosecution, defense, settlement, arbitration and appeal of, and the giving of testimony in, any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative.

(2) The term "expenses" shall be broadly construed and shall include, without limitation, court costs, attorneys' fees, witness fees, fines, amounts paid in settlement or judgment and any other costs and expenses of any nature or kind incurred in connection with any proceeding.

(3) The term the "corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under the provisions of this Section 43 with respect to the resulting or surviving corporation as he would have with respect to such constituent corporation if its separate existence had continued.

(4) References to a "director," "executive officer," "officer," "employee," or "agent" of the corporation shall include, without limitation, situations where such person is serving at the request of the corporation as, respectively, a director, executive officer, officer, employee, trustee or agent of another corporation, partnership, joint venture, trust or other enterprise.

(5) References to "other enterprises" shall include employee benefit plans; references to "fines" shall include any excise taxes assessed on a person with respect to an employee benefit plan; and references to "serving at the request of the corporation" shall include any service as a director, officer, employee or agent of the corporation which imposes duties on, or involves services by, such director, officer, employee, or agent with respect to an employee benefit plan, its participants, or beneficiaries; and a person who acted in good faith and in a manner he reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner "not opposed to the best interests of the corporation" as referred to in this Section 43.

ARTICLE XII

NOTICES

SECTION 44. NOTICES.

(a) NOTICE TO STOCKHOLDERS. Whenever, under any provisions of these Bylaws, notice is required to be given to any stockholder, it shall be given in writing, timely and duly deposited in the United States mail, postage prepaid, and addressed to his last known post office address as shown by the stock record of the corporation or its transfer agent.

(b) NOTICE TO DIRECTORS. Any notice required to be given to any director may be given by the method stated in subsection (a), or by overnight delivery service, facsimile, telex or telegram, except that such notice other than one which is delivered personally shall be sent to such address as such director shall have filed in writing with the Secretary, or, in the absence of such filing, to the last known post office address of such director.

(c) AFFIDAVIT OF MAILING. An affidavit of mailing, executed by a duly authorized and competent employee of the corporation or its transfer agent appointed with respect to the class of stock affected, specifying the name and address or the names and

addresses of the stockholder or stockholders, or director or directors, to whom any such notice or notices was or were given, and the time and method of giving the same, shall in the absence of fraud, be prima facie evidence of the facts therein contained.

(d) TIME NOTICES DEEMED GIVEN. All notices given by mail or by overnight delivery service, as above provided, shall be deemed to have been given as at the time of mailing, and all notices given by facsimile, telex or telegram shall be deemed to have been given as of the sending time recorded at time of transmission.

(e) METHODS OF NOTICE. It shall not be necessary that the same method of giving notice be employed in respect of all directors, but one permissible method may be employed in respect of any one or more, and any other permissible method or methods may be employed in respect of any other or others.

(f) FAILURE TO RECEIVE NOTICE. The period or limitation of time within which any stockholder may exercise any option or right, or enjoy any privilege or benefit, or be required to act, or within which any director may exercise any power or right, or enjoy any privilege, pursuant to any notice sent him in the manner above provided, shall not be affected or extended in any manner by the failure of such stockholder or such director to receive such notice.

(g) NOTICE TO PERSON WITH WHOM COMMUNICATION IS UNLAWFUL. Whenever notice is required to be given, under any provision of law or of the Certificate of Incorporation or Bylaws of the corporation, to any person with whom communication is unlawful, the giving of such notice to such person shall not be required and there shall be no duty to apply to any governmental authority or agency for a license or permit to give such notice to such person. Any action or meeting which shall be taken or held without notice to any such person with whom communication is unlawful shall have the same force and effect as if such notice had been duly given. In the event that the action taken by the corporation is such as to require the filing of a certificate under any provision of the DGCL, the certificate shall state, if such is the fact and if notice is required, that notice was given to all persons entitled to receive notice except such persons with whom communication is unlawful.

(h) NOTICE TO PERSON WITH UNDELIVERABLE ADDRESS. Whenever notice is required to be given, under any provision of law or the Certificate of Incorporation or Bylaws of the corporation, to any stockholder to whom (i) notice of two consecutive annual meetings, and all notices of meetings or of the taking of action by written consent without a meeting to such person during the period between such two consecutive annual meetings, or (ii) all, and at least two, payments (if sent by first class mail) of dividends or interest on securities during a twelve-month period, have been mailed addressed to such person at his address as shown on the records of the corporation and have been returned undeliverable, the giving of such notice to such person shall not be required. Any action or meeting which shall be taken or held without notice to such person shall have the same force and effect as if such notice had been duly given. If any such person shall deliver to the corporation a written notice setting forth his then current address, the requirement that notice be given to such person shall be reinstated. In the event that the action taken by the corporation is such as to require the filing of a certificate under any provision of the DGCL, the certificate need not state that notice was not given to persons to whom notice was not required to be given pursuant to this paragraph.

ARTICLE XIII

AMENDMENTS

SECTION 45. AMENDMENTS. Subject to paragraph (h) of Section 43 of the Bylaws, the Bylaws may be altered or amended or new Bylaws adopted by the affirmative vote of at least sixty-six and two-thirds percent (66-2/3%) of the voting power of all of the then-outstanding shares of the voting stock of the corporation entitled to vote. The Board of Directors shall also have the power to adopt, amend, or repeal Bylaws.

ARTICLE XIV

LOANS TO OFFICERS

SECTION 45. LOANS TO OFFICERS. The corporation may lend money to, or guarantee any obligation of, or otherwise assist any officer or other employee of the corporation or of its subsidiaries, including any officer or employee who is a Director of the corporation or its subsidiaries, whenever, in the judgment of the Board of Directors, such loan, guarantee or assistance may reasonably be expected to benefit the corporation. The loan, guarantee or other assistance may be with or without interest and may be unsecured, or secured in such manner as the Board of Directors shall approve, including, without limitation, a pledge of shares of stock of the corporation. Nothing in these Bylaws shall be deemed to deny, limit or restrict the powers of guaranty or warranty of the corporation at common law or under any statute.

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EXHIBIT 4.1

COMMON SHARES COMMON SHARES

RGL
RIGEL PHARMACEUTICALS, INC.

INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE

CUSIP 766559 10 8

SEE REVERSE FOR CERTAIN DEFINITIONS

This Certifies that is the record holder of

FULLY PAID AND NON-ASSESSABLE SHARES OF THE COMMON STOCK,
PAR VALUE $0.001 PER SHARE, OF
RIGEL PHARMACEUTICALS, INC.

transferable only on the books of the Corporation by the holder hereof in person or by duly authorized Attorney upon surrender of this Certificate properly endorsed. This Certificate is not valid unless countersigned and registered by the Transfer Agent and Registrar.

In Witness Whereof, the Corporation has caused this Certificate to be executed and attested to by the manual or facsimile signatures of its duly authorized officers, under a facsimile of its corporate seal to be affixed hereto.

Dated:

SENIOR VICE PRESIDENT, CHIEF OPERATING OFFICER,
CHIEF FINANCIAL OFFICER AND SECRETARY
PRESIDENT AND
CHIEF EXECUTIVE OFFICER

Countersigned and Registered:
Wells Fargo Bank Minnesota, N.A.,
Transfer Agent
and Registrar

By:
Authorized Officer

RIGEL PHARMACEUTICALS, INC.

Upon request the Corporation will furnish any holder of shares of Common Stock of the Corporation, without charge, with a full statement of the powers, designations, preferences, and relative, participating, optional or other special rights of any class or series of capital stock of the Corporation, and the qualifications, limitations or restrictions of such preferences and/or rights.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM	N	as tenants in common
TEN ENT	N	as tenants by the entireties
JT TEN	N	as joint tenants with right of survivorship and not as tenants in common

UNIF GIFT MIN ACT N ..... Custodian .....
(Cust) (Minor)
under Uniform Gifts to Minors
Act .....
(State)

Additional abbreviations may also be used though not in the above list.
For value received,_____ hereby sell, assign and transfer unto

PLEASE INSERT SOCIAL SECURITY OR OTHER
IDENTIFYING NUMBER OF ASSIGNEE

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING ZIP CODE OF ASSIGNEE)

_____Shares of Common Stock represented by the within Certificate, and do hereby irrevocably constitute and appoint_____ Attorney to transfer the said stock on the books of the within named Corporation with full power of substitution in the premises.

Dated

In presence of
X
X

NOTICE
THE SIGNATURE(S) TO THIS ASSIGNMENT MUST CORRESPOND WITH THE NAME AS WRITTEN UPON THE FACE OF THE CERTIFICATE IN EVERY PARTICULAR, WITHOUT ALTERATION OR ENLARGEMENT OR ANY CHANGE WHATEVER.

Signature(s) Guaranteed

By
THE SIGNATURE(S) MUST BE GUARANTEED BY AN ELIGIBLE GUARANTOR INSTITUTION (BANKS, STOCKBROKERS, SAVINGS AND LOAN ASSOCIATIONS AND CREDIT UNIONS WITH MEMBERSHIP IN AN APPROVED SIGNATURE GUARANTEE MEDALLION PROGRAM), PURSUANT TO SEC RULE 17Ad-15.

Exhibit 4.2

RIGEL PHARMACEUTICALS, INC.

AMENDED AND RESTATED

INVESTOR RIGHTS AGREEMENT

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RIGEL PHARMACEUTICALS, INC.

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT

THIS AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT (the "Agreement") is entered into as of February 3, 2000, by and among RIGEL PHARMACEUTICALS, INC., a Delaware corporation (the "Company"), the holders of the Company's Series B Preferred Stock ("Series B Stock"), Series C Preferred Stock ("Series C Stock") and Series D Preferred Stock ("Series D Stock"), set forth on the Schedule of Investors attached hereto as Schedule A, and the purchasers of the Company's Series E Preferred Stock ("Series E Stock") set forth on Schedule A of that certain Series E Preferred Stock Purchase Agreement of even date herewith (the "Purchase Agreement") and Schedule A hereto together, the "Investors" and each individually, an "Investor."

RECITALS

WHEREAS, certain of the Investors hold shares of the Company's Series B Stock, Series C Stock, Series D Stock and/or shares of Common Stock issued upon conversion thereof and possess registration rights, information rights, and other rights pursuant to that certain Amended and Restated Investor Rights Agreement dated as of December 18, 1998 (as amended May 26, 1999), between the Company and such Investors (the "Prior Agreement"); and

WHEREAS, the Investors who hold Series B Stock, Series C Stock and Series D Stock desire to terminate the Prior Agreement and to accept the rights created pursuant hereto in lieu of the rights granted to them under the Prior Agreement; and

WHEREAS, the Company proposes to sell and issue up to Two Million Seven Hundred Fifty Thousand (2,750,000) shares of its Series E Stock pursuant to the Purchase Agreement; and

WHEREAS, as a condition of entering into the Purchase Agreement, certain of the Investors who are parties to such Purchase Agreement have requested that the Company extend to them registration rights, information rights and other rights as set forth below.

NOW, THEREFORE, in consideration of the mutual promises, representations, warranties, covenants and conditions set forth herein, the Investors who are parties to the Prior Agreement hereby agree that the Prior Agreement shall be superseded and replaced in its entirety by this Agreement and the parties hereto mutually agree as follows:

SECTION 1. GENERAL

1.1 DEFINITIONS. As used in this Agreement the following terms shall have the following respective meanings:

"EXCHANGE ACT" means the Securities Exchange Act of 1934, as amended.

"HOLDER" means any person owning of record Registrable Securities that have not been sold to the public or any assignee of record of such Registrable Securities in accordance with Section 2.10 hereof.

"INITIAL OFFERING" means the Company's first firm commitment underwritten public offering of its Common Stock registered under the Securities Act.

"REGISTER," "registered," and "registration" refer to a registration effected by preparing and filing a registration statement in compliance with the Securities Act, and the declaration or ordering of effectiveness of such registration statement or document.

"REGISTRABLE SECURITIES" means (i) Common Stock of the Company issued or issuable upon conversion of the Shares; and (ii) any Common Stock of the Company issued as (or issuable upon the conversion or exercise of any warrant, right or other security which is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, such above-described securities. Notwithstanding the foregoing, Registrable Securities shall not include any securities sold by a person to the public either pursuant to a registration statement or Rule 144 or sold in a private transaction in which the transferor's rights under Section 2 of this Agreement are not assigned.

"REGISTRABLE SECURITIES THEN OUTSTANDING" shall be the number of shares determined by calculating the total number of shares of the Company's Common Stock that are Registrable Securities and either (1) are then issued and outstanding or (2) are issuable pursuant to then exercisable or convertible securities.

"REGISTRATION EXPENSES" shall mean all expenses incurred by the Company in complying with Sections 2.2, 2.3 and 2.4 hereof, including, without limitation, all registration and filing fees, printing expenses, fees and disbursements of counsel for the Company, reasonable fees and disbursements not to exceed Fifteen Thousand Dollars ($15,000) of a single special counsel for the Holders, blue sky fees and expenses and the expense of any special audits incident to or required by any such registration (but excluding the compensation of regular employees of the Company which shall be paid in any event by the Company).

"SECURITIES ACT" shall mean the Securities Act of 1933, as amended.

"SELLING EXPENSES" shall mean all underwriting discounts and selling commissions applicable to the sale.

"SHARES" shall mean the Company's Series B Stock issued pursuant to the Series B Preferred Stock Purchase Agreement dated January 22, 1997 and the Investors listed on Schedule A thereto and their permitted assigns, Series C Stock issued pursuant to the Series C Preferred Stock Purchase Agreement dated November 3, 1997 and the Investors listed on Schedule A thereto and their permitted assigns, Series D Stock issued pursuant to the Series D Preferred Stock Purchase Agreement dated December 18, 1998 (as amended May 26, 1999) and the Investors listed on Schedule A thereto and their permitted assigns and Series E Stock issued

pursuant to the Purchase Agreement and held by the Investors listed on Schedule A thereto and their permitted assigns.

"FORM S-3" means such form under the Securities Act as in effect on the date hereof or any successor registration form under the Securities Act subsequently adopted by the SEC which permits inclusion or incorporation of

substantial information by reference to other documents filed by the Company with the SEC.

"SEC" OR "COMMISSION" means the Securities and Exchange Commission.

SECTION 2. REGISTRATION; RESTRICTIONS ON TRANSFER

2.1 RESTRICTIONS ON TRANSFER.

(a) Each Holder agrees not to make any disposition of all or any portion of the Shares or Registrable Securities unless and until:

(i) There is then in effect a registration statement under the Securities Act covering such proposed disposition and such disposition is made in accordance with such registration statement; or

(ii) (A) The transferee has agreed in writing to be bound by the terms of this Agreement, (B) such Holder shall have notified the Company of the proposed disposition and shall have furnished the Company with a statement of the circumstances surrounding the proposed disposition, and (C) if reasonably requested by the Company, such Holder shall have furnished the Company with an opinion of counsel, reasonably satisfactory to the Company, that such disposition will not require registration of such shares under the Securities Act. It is agreed that the Company will not require opinions of counsel for transactions made pursuant to Rule 144 except in unusual circumstances.

(iii) Notwithstanding the provisions of paragraphs (i) and (ii) above, no such registration statement or opinion of counsel shall be necessary for a transfer by a Holder which is (A) a partnership to its partners or former partners in accordance with partnership interests, (B) a corporation to its stockholders in accordance with their interest in the corporation, (C) a limited liability company to its members or former members in accordance with their interest in the limited liability company, or (D) to the Holder's family member or trust for the benefit of an individual Holder or his or her family member; provided that in each case the transferee will be subject to the terms of this Agreement to the same extent as if he or she were an original Holder hereunder.

(b) Each certificate representing Shares or Registrable Securities shall (unless otherwise permitted by the provisions of the Purchase Agreement) be stamped or otherwise imprinted with a legend substantially similar to the following (in addition to any legend required under applicable state securities laws or as provided elsewhere in this Agreement):

The following legend under the Securities Act:

THE SHARES REPRESENTED HEREBY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND MAY NOT BE SOLD, TRANSFERRED, ASSIGNED, PLEDGED OR HYPOTHECATED UNLESS AND UNTIL REGISTERED UNDER SUCH ACT, OR UNLESS THE COMPANY HAS RECEIVED AN OPINION OF COUNSEL OR OTHER EVIDENCE, SATISFACTORY TO THE COMPANY AND ITS COUNSEL, THAT SUCH REGISTRATION IS NOT REQUIRED.

(c) The Company shall be obligated to reissue promptly unlegended certificates at the request of any holder thereof if the holder shall have obtained an opinion of counsel (which counsel may be counsel to the Company) reasonably acceptable to the Company to the effect that the securities proposed to be disposed of may lawfully be so disposed of without registration, qualification or legend.

(d) Any legend endorsed on an instrument pursuant to applicable state securities laws and the stop-transfer instructions with respect to such securities shall be removed upon receipt by the Company of an order of the appropriate blue sky authority authorizing such removal.

2.2 DEMAND REGISTRATION.

(a) Subject to the conditions of this Section 2.2, if the Company shall receive a written request from the Holders of more than fifty percent (50%) of the Registrable Securities then outstanding (the "Initiating Holders") that the Company file a registration statement under the Securities Act covering the registration of Registrable Securities having an aggregate offering price to the public in excess of $5,000,000 (a "Qualified Public Offering"), then the Company shall, within thirty (30) days of the receipt thereof, give written notice of such request to all Holders, and subject to the limitations of this Section 2.2, use its best efforts to effect, as soon as practicable, the registration under the Securities Act of all Registrable Securities that the Holders request to be registered.

(b) If the Initiating Holders intend to distribute the

Registrable Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to this Section 2.2 or any request pursuant to Section 2.4 and the Company shall include such information in the written notice referred to in Section 2.2(a) or Section 2.4(a), as applicable. In such event, the right of any Holder to include its Registrable Securities in such registration shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting (unless otherwise mutually agreed by a majority in interest of the Initiating Holders and such Holder) to the extent provided herein. All Holders proposing to distribute their securities through such underwriting shall enter into an underwriting agreement in customary form with the

underwriter or underwriters selected for such underwriting by a majority in interest of the Initiating Holders (which underwriter or underwriters shall be reasonably acceptable to the Company). Notwithstanding any other provision of this Section 2.2 or Section 2.4, if the underwriter advises the Company that marketing factors require a limitation of the number of securities to be underwritten (including Registrable Securities) then the Company shall so advise all Holders of Registrable Securities which would otherwise be underwritten pursuant hereto, and the number of shares that may be included in the underwriting shall be allocated, first, to the Initiating Holders and, second, to all other Holders of such Registrable Securities on a pro rata basis based on the total number of Registrable Securities held by all such Holders. Any Registrable Securities excluded or withdrawn from such underwriting shall be withdrawn from the registration.

(c) The Company shall not be required to effect a registration pursuant to this Section 2.2:

(i) prior to the fourth anniversary of the date of this Agreement;

(ii) after the Company has effected two (2) registrations pursuant to this Section 2.2, and such registrations have been declared or ordered effective;

(iii) during the period starting with the date of filing of, and ending on the date one hundred eighty (180) days following the effective date of the registration statement pertaining to the Initial Offering; provided that the Company makes reasonable good faith efforts to cause such registration statement to become effective;

(iv) if within thirty (30) days of receipt of a written request from Initiating Holders pursuant to Section 2.2(a), the Company gives notice to the Holders of the Company's intention to make its Initial Offering within ninety (90) days; or

(v) if the Company shall furnish to Holders requesting a registration statement pursuant to this Section 2.2, a certificate signed by the Chairman of the Board stating that in the good faith judgment of the Board of Directors of the Company, it would be seriously detrimental to the Company and its stockholders for such registration statement to be effected at such time, in which event the Company shall have the right to defer such filing for a period of not more than ninety (90) days after receipt of the request of the Initiating Holders; provided that such right to delay a request shall be exercised by the Company not more than once in any twelve (12) month period.

2.3 PIGGYBACK REGISTRATIONS. The Company shall notify all Holders of Registrable Securities in writing at least thirty (30) days prior to the filing of any registration statement under the Securities Act for purposes of a public offering of securities of the Company (including a registration statement filed pursuant to Section 2.2 of this Agreement and including, but not limited to, registration statements relating to secondary offerings of securities of the Company, but excluding registration statements relating to employee benefit plans or with respect to corporate reorganizations or other transactions under Rule 145 of the Securities Act) and will afford each such Holder an opportunity to include in such registration statement all or part of

such Registrable Securities held by such Holder. Each Holder desiring to include in any such registration statement all or any part of the Registrable Securities held by it shall, within fifteen (15) days after the above-described notice from the Company, so notify the Company in writing. Such notice shall state the intended method of disposition of the Registrable Securities by such Holder. If a Holder decides not to include all of its Registrable Securities in any registration statement thereafter filed by the Company, such Holder shall nevertheless continue to have the right to include any Registrable Securities in

any subsequent registration statement or registration statements as may be filed by the Company with respect to offerings of its securities, all upon the terms and conditions set forth herein.

(a) UNDERWRITING. If the registration statement under which the Company gives notice under this Section 2.3 is for an underwritten offering, the Company shall so advise the Holders of Registrable Securities. In such event, the right of any such Holder to be included in a registration pursuant to this Section 2.3 shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such Holder's Registrable Securities in the underwriting to the extent provided herein. All Holders proposing to distribute their Registrable Securities through such underwriting shall enter into an underwriting agreement in customary form with the underwriter or underwriters selected for such underwriting by the Company. Notwithstanding any other provision of this Agreement, if the underwriter determines in good faith that marketing factors require a limitation of the number of shares to be underwritten, the number of shares that may be included in the underwriting shall be allocated, first, to the Company (or in the case of a registration pursuant to Section 2.2, the Initiating Holders); second, to the Holders on a pro rata basis based on the total number of Registrable Securities held by the Holders; and third, to any stockholder of the Company (other than a Holder) on a pro rata basis. No such reduction shall (i) reduce the securities being offered by the Company for its own account to be included in the registration and underwriting, or (ii) reduce the amount of securities of the selling Holders included in the registration below twenty-five percent (25%) of the total amount of securities included in such registration, unless such offering is the Initial Offering and such registration does not include shares of any other selling stockholders, in which event any or all of the Registrable Securities of the Holders may be excluded in accordance with the immediately preceding sentence. In no event will shares of any other selling stockholder be included in such registration which would reduce the number of shares which may be included by Holders without the written consent of Holders of not less than two-thirds (66 2/3%) of the Registrable Securities proposed to be sold in the offering.

(b) RIGHT TO TERMINATE REGISTRATION. The Company shall have the right to terminate or withdraw any registration initiated by it under this Section 2.3 prior to the effectiveness of such registration whether or not any Holder has elected to include securities in such registration. The Registration Expenses of such withdrawn registration shall be borne by the Company in accordance with Section 2.5 hereof.

2.4 FORM S-3 REGISTRATION. In case the Company shall receive from any Holder or Holders of Registrable Securities a written request or requests that the Company effect a registration on Form S-3 (or any successor to Form S-3) or any similar short-form registration

statement and any related qualification or compliance with respect to all or a part of the Registrable Securities owned by such Holder or Holders, the Company will:

(a) promptly give written notice of the proposed registration, and any related qualification or compliance, to all other Holders of Registrable Securities; and

(b) as soon as practicable, effect such registration and all such qualifications and compliances as may be so requested and as would permit or facilitate the sale and distribution of all or such portion of such Holder's or Holders' Registrable Securities as are specified in such request, together with all or such portion of the Registrable Securities of any other Holder or Holders joining in such request as are specified in a written request given within fifteen (15) days after receipt of such written notice from the Company; provided, however, that the Company shall not be obligated to effect any such registration, qualification or compliance pursuant to this Section 2.4:

(i) if Form S-3 (or any successor or similar form) is not available for such offering by the Holders, or

(ii) if the Holders, together with the holders of any other securities of the Company entitled to inclusion in such registration, propose to sell Registrable Securities and such other securities (if any) at an aggregate price to the public of less than $500,000, or

(iii) if the Company shall furnish to the Holders a certificate signed by the Chairman of the Board of Directors of the Company stating that in the good faith judgment of the Board of Directors of the Company, it would be seriously detrimental to the Company and its stockholders for such Form S-3 Registration to be effected at such time, in which event the Company shall have the right to defer the filing of the Form S-3 registration statement for a period of not more than ninety (90) days after receipt of the request of the Holder or Holders under this Section 2.4: provided, that such right to delay a request shall be exercised by the Company not more than once in

any twelve (12) month period, or

(iv) if the Company has, within the twelve (12) month period preceding the date of such request, already effected two (2) registrations on Form S-3 for the Holders pursuant to this Section 2.4, or

(v) if the Company has already effected three (3) registrations on Form S-3 for the Holders pursuant to this Section 2.4, or

(vi) in any particular jurisdiction in which the Company would be required to qualify to do business or to execute a general consent to service of process in effecting such registration, qualification or compliance.

(c) Subject to the foregoing, the Company shall file a Form S-3 registration statement covering the Registrable Securities and other securities so requested to be registered as soon as practicable after receipt of the request or requests of the Holders.

2.5 EXPENSES OF REGISTRATION. Except as specifically provided herein, all Registration Expenses incurred in connection with any registration, qualification or compliance pursuant to Section 2.2, Section 2.3 or Section 2.4 herein shall be borne by the Company. All Selling Expenses incurred in connection with any registrations hereunder, shall be borne by the holders of the securities so registered pro rata on the basis of the number of shares so registered. The Company shall not, however, be required to pay for expenses of any registration proceeding begun pursuant to Section 2.2 or 2.4, the request of which has been subsequently withdrawn by the Initiating Holders unless (a) the withdrawal is based upon material adverse information concerning the Company of which the Initiating Holders were not aware at the time of such request or (b) the Holders of a majority of Registrable Securities agree to forfeit their right to one requested registration pursuant to Section 2.2 or Section 2.4, as applicable, in which event such right shall be forfeited by all Holders. If the Holders are required to pay the Registration Expenses, such expenses shall be borne by the holders of securities (including Registrable Securities) requesting such registration in proportion to the number of shares for which registration was requested. If the Company is required to pay the Registration Expenses of a withdrawn offering pursuant to clause (a) above, then the Holders shall not forfeit their rights pursuant to Section 2.2 or Section 2.4 to a demand or S-3 registration.

2.6 OBLIGATIONS OF THE COMPANY. Whenever required to effect the registration of any Registrable Securities, the Company shall, as expeditiously as reasonably possible:

(a) Prepare and file with the SEC a registration statement with respect to such Registrable Securities and use all reasonable efforts to cause such registration statement to become effective, and, upon the request of the Holders of a majority of the Registrable Securities registered thereunder, keep such registration statement effective for up to ninety (90) days or, if earlier, until the Holder or Holders have completed the distribution related thereto.

(b) Prepare and file with the SEC such amendments and supplements to such registration statement and the prospectus used in connection with such registration statement as may be necessary to comply with the provisions of the Securities Act with respect to the disposition of all securities covered by such registration statement.

(c) Furnish to the Holders such number of copies of a prospectus, including a preliminary prospectus, in conformity with the requirements of the Securities Act, and such other documents as they may reasonably request in order to facilitate the disposition of Registrable Securities owned by them.

(d) Use all reasonable efforts to register and qualify the securities covered by such registration statement under such other securities or Blue Sky laws of such jurisdictions as shall be reasonably requested by the Holders, provided that the Company shall not be required in connection therewith or as a condition thereto to qualify to do business or to file a general consent to service of process in any such states or jurisdictions.

(e) In the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the managing

underwriter(s) of such offering. Each Holder participating in such underwriting shall also enter into and perform its obligations under such an agreement.

(f) Notify each Holder of Registrable Securities covered by such

registration statement at any time when a prospectus relating thereto is required to be delivered under the Securities Act of the happening of any event as a result of which the prospectus included in such registration statement, as then in effect, includes an untrue statement of a material fact or omits to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances then existing.

(g) Furnish, at the request of a majority of the Holders participating in the registration, on the date that such Registrable Securities are delivered to the underwriters for sale, if such securities are being sold through underwriters, or, if such securities are not being sold through underwriters, on the date that the registration statement with respect to such securities becomes effective, (i) an opinion, dated as of such date, of the counsel representing the Company for the purposes of such registration, in form and substance as is customarily given to underwriters in an underwritten public offering and reasonably satisfactory to a majority in interest of the Holders requesting registration, addressed to the underwriters, if any, and to the Holders requesting registration of Registrable Securities and (ii) a letter dated as of such date, from the independent certified public accountants of the Company, in form and substance as is customarily given by independent certified public accountants to underwriters in an underwritten public offering and reasonably satisfactory to a majority in interest of the Holders requesting registration, addressed to the underwriters, if any, and if permitted by applicable accounting standards, to the Holders requesting registration of Registrable Securities.

2.7 TERMINATION OF REGISTRATION RIGHTS. All registration rights granted under this Section 2 shall terminate and be of no further force and effect three (3) years after the date of the Company's Initial Offering. In addition, a Holder's registration rights shall expire if (i) the Company has completed its Initial Offering and is subject to the provisions of the Exchange Act, (ii) such Holder (together with its affiliates, partners and former partners) holds less than 1% of the Company's outstanding Common Stock (treating all shares of convertible Preferred Stock on an as-converted basis) and (iii) all Registrable Securities held by and issuable to such Holder (and its affiliates, partners and former partners) may be sold under Rule 144 during any ninety (90) day period.

2.8 DELAY OF REGISTRATION; FURNISHING INFORMATION.

(a) It shall be a condition precedent to the obligations of the Company to take any action pursuant to Section 2.2, 2.3 or 2.4 that the selling Holders shall furnish to the Company such information regarding themselves, the Registrable Securities held by them and the intended method of disposition of such securities as shall be required to effect the registration of their Registrable Securities.

(b) The Company shall have no obligation with respect to any registration requested pursuant to Section 2.2 or Section 2.4 if, due to the operation of subsection 2.2(b), the number of shares or the anticipated aggregate offering price of the Registrable Securities to be

included in the registration does not equal or exceed the number of shares or the anticipated aggregate offering price required to originally trigger the Company's obligation to initiate such registration as specified in Section 2.2 or Section 2.4, whichever is applicable.

2.9 INDEMNIFICATION. In the event any Registrable Securities are included in a registration statement under Sections 2.2, 2.3 or 2.4:

(a) To the extent permitted by law, the Company will indemnify and hold harmless each Holder, the partners, officers, directors and legal counsel of each Holder, any underwriter (as defined in the Securities Act) for such Holder and each person, if any, who controls such Holder or underwriter within the meaning of the Securities Act or the Exchange Act, against any losses, claims, damages, or liabilities (joint or several) to which they may become subject under the Securities Act, the Exchange Act or other federal or state law, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon any of the following statements, omissions or violations (collectively a "Violation") by the Company: (i) any untrue statement or alleged untrue statement of a material fact contained in such registration statement, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto, (ii) the omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading, or (iii) any violation or alleged violation by the Company of the Securities Act, the Exchange Act, any state securities law or any rule or regulation promulgated under the Securities Act, the Exchange Act or any state securities law in connection with the offering covered by such registration statement; and the Company will reimburse each such Holder, partner, officer or director, underwriter or controlling person for any legal or other expenses reasonably

incurred by them in connection with investigating or defending any such loss, claim, damage, liability or action; provided however, that the indemnity agreement contained in this Section 2.9(a) shall not apply to amounts paid in settlement of any such loss, claim, damage, liability or action if such settlement is effected without the consent of the Company, which consent shall not be unreasonably withheld, nor shall the Company be liable in any such case for any such loss, claim, damage, liability or action to the extent that it arises out of or is based upon a Violation which occurs in reliance upon and in conformity with written information furnished expressly for use in connection with such registration by such Holder, partner, officer, director, underwriter or controlling person of such Holder.

(b) To the extent permitted by law, each Holder will, if Registrable Securities held by such Holder are included in the securities as to which such registration, qualification or compliance is being effected, indemnify and hold harmless the Company, each of its directors, its officers, and legal counsel and each person, if any, who controls the Company within the meaning of the Securities Act, any underwriter and any other Holder selling securities under such registration statement or any of such other Holder's partners, directors or officers or any person who controls such Holder, against any losses, claims, damages or liabilities (joint or several) to which the Company or any such director, officer, controlling person, underwriter or other such Holder, or partner, director, officer or controlling person of such other Holder may become subject under the Securities Act, the Exchange Act or other federal or state law, insofar as such losses, claims, damages or liabilities (or actions in respect thereto) arise out of or are based upon

any Violation, in each case to the extent (and only to the extent) that such Violation occurs in reliance upon and in conformity with written information furnished by such Holder under an instrument duly executed by such Holder and stated to be specifically for use in connection with such registration; and each such Holder will reimburse any legal or other expenses reasonably incurred by the Company or any such director, officer, controlling person, underwriter or other Holder, or partner, officer, director or controlling person of such other Holder in connection with investigating or defending any such loss, claim, damage, liability or action if it is judicially determined that there was such a Violation; provided, however, that the indemnity agreement contained in this Section 2.9(b) shall not apply to amounts paid in settlement of any such loss, claim, damage, liability or action if such settlement is effected without the consent of the Holder, which consent shall not be unreasonably withheld; provided further, that in no event shall any indemnity under this Section 2.9 exceed the proceeds from the offering received by such Holder.

(c) Promptly after receipt by an indemnified party under this Section 2.9 of notice of the commencement of any action (including any governmental action), such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Section 2.9, deliver to the indemnifying party a written notice of the commencement thereof and the indemnifying party shall have the right to participate in, and, to the extent the indemnifying party so desires, jointly with any other indemnifying party similarly noticed, to assume the defense thereof with counsel mutually satisfactory to the parties; provided, however, that an indemnified party shall have the right to retain its own counsel, with the fees and expenses to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such proceeding. The failure to deliver written notice to the indemnifying party within a reasonable time of the commencement of any such action, if materially prejudicial to its ability to defend such action, shall relieve such indemnifying party of any liability to the indemnified party under this Section 2.9, but the omission so to deliver written notice to the indemnifying party will not relieve it of any liability that it may have to any indemnified party otherwise than under this Section 2.9.

(d) If the indemnification provided for in this Section 2.9 is held by a court of competent jurisdiction to be unavailable to an indemnified party with respect to any losses, claims, damages or liabilities referred to herein, the indemnifying party, in lieu of indemnifying such indemnified party thereunder, shall to the extent permitted by applicable law contribute to the amount paid or payable by such indemnified party as a result of such loss, claim, damage or liability in such proportion as is appropriate to reflect the relative fault of the indemnifying party on the one hand and of the indemnified party on the other in connection with the Violation(s) that resulted in such loss, claim, damage or liability, as well as any other relevant equitable considerations. The relative fault of the indemnifying party and of the indemnified party shall be determined by a court of law by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission to state a material fact relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or

omission; provided, that in no event shall any contribution by a Holder hereunder exceed the proceeds from the offering received by such Holder.

(e) The obligations of the Company and Holders under this Section 2.9 shall survive completion of any offering of Registrable Securities in a registration statement and the termination of this Agreement. No Indemnifying Party, in the defense of any such claim or litigation, shall, except with the consent of each Indemnified Party, consent to entry of any judgment or enter into any settlement which does not include as an unconditional term thereof the giving by the claimant or plaintiff to such Indemnified Party of a release from all liability in respect to such claim or litigation.

2.10 ASSIGNMENT OF REGISTRATION RIGHTS. The rights to cause the Company to register Registrable Securities pursuant to this Section 2 may be assigned by a Holder to a transferee or assignee of Registrable Securities which (i) is a general partner, limited partner or retired partner of a Holder, (ii) is a Holder's family member or trust for the benefit of an individual Holder or family member, or (iii) acquires at least three hundred thousand (300,000) shares of Registrable Securities (as adjusted for stock splits and combinations); provided, however, (A) the transferor shall, within ten (10) days after such transfer, furnish to the Company written notice of the name and address of such transferee or assignee and the securities with respect to which such registration rights are being assigned and (B) such transferee shall agree to be subject to all restrictions set forth in this Agreement.

2.11 AMENDMENT OF REGISTRATION RIGHTS. Any provision of this Section 2 may be amended and the observance thereof may be waived (either generally or in a particular instance and either retroactively or prospectively), only with the written consent of the Company and the Holders of at least sixty-six and two-thirds percent (66 2/3%) of the Registrable Securities then outstanding. Any amendment or waiver effected in accordance with this Section 2.11 shall be binding upon each Holder and the Company.

2.12 LIMITATION ON SUBSEQUENT REGISTRATION RIGHTS. After the date of this Agreement, the Company shall not, without the prior written consent of the Holders of sixty-six and two-thirds percent (66 2/3%) of the Registrable Securities then outstanding, enter into any agreement with any holder or prospective holder of any securities of the Company that would grant such holder registration rights senior to or on parity with those granted to the Holders hereunder.

2.13 "MARKET STAND-OFF" AGREEMENT. Each Holder hereby agrees that such Holder shall not sell or otherwise transfer or dispose of any Common Stock (or other securities) of the Company held by such Holder (other than those included in the registration) for a period specified by the representative of the underwriters of Common Stock (or other securities) of the Company not to exceed one hundred eighty (180) days following the effective date of a registration statement of the Company filed under the Securities Act, provided that:

(i) such agreement shall apply only to the Company's Initial Offering; and

(ii) all officers and directors of the Company and holders of at least three percent (3%) of the Company's voting securities enter into similar agreements.

Each Holder agrees to execute and deliver such other agreements as may be reasonably requested by the Company or the underwriter which are consistent with the foregoing or which are necessary to give further effect thereto. The obligations described in this Section 2.13 shall not apply to a registration relating solely to employee benefit plans on Form S-1 or Form S-8 or similar forms that may be promulgated in the future, or a registration relating solely to a Commission Rule 145 transaction on Form S-4 or similar forms that may be promulgated in the future. The Company may impose stop-transfer instructions with respect to the shares of Common Stock (or other securities) subject to the foregoing restriction until the end of said one hundred eighty (180) day period.

2.14 RULE 144 REPORTING. With a view to making available to the Holders the benefits of certain rules and regulations of the SEC which may permit the sale of the Registrable Securities to the public without registration, the Company agrees to use its best efforts to:

(a) Make and keep public information available, as those terms are understood and defined in SEC Rule 144 or any similar or analogous rule promulgated under the Securities Act, at all times after the effective date of the first registration filed by the Company for an offering of its securities to

the general public;

(b) File with the SEC, in a timely manner, all reports and other documents required of the Company under the Exchange Act;

(c) So long as a Holder owns any Registrable Securities, furnish to such Holder forthwith upon request: a written statement by the Company as to its compliance with the reporting requirements of said Rule 144 of the Securities Act, and of the Exchange Act (at any time after it has become subject to such reporting requirements); a copy of the most recent annual or quarterly report of the Company; and such other reports and documents as a Holder may reasonably request in availing itself of any rule or regulation of the SEC allowing it to sell any such securities without registration.

SECTION 3. COVENANTS OF THE COMPANY

3.1 BASIC FINANCIAL INFORMATION AND REPORTING.

(a) The Company will maintain true books and records of account in which full and correct entries will be made of all its business transactions pursuant to a system of accounting established and administered in accordance with generally accepted accounting principles consistently applied, and will set aside on its books all such proper accruals and reserves as shall be required under generally accepted accounting principles consistently applied.

(b) As soon as practicable after the end of each fiscal year of the Company, and in any event within ninety (90) days thereafter, the Company will furnish each Investor a consolidated balance sheet of the Company, as at the end of such fiscal year, and a consolidated

statement of income and a consolidated statement of cash flows of the Company, for such year, all prepared in accordance with generally accepted accounting principles consistently applied and setting forth in each case in comparative form the figures for the previous fiscal year, all in reasonable detail. Such financial statements shall be accompanied by a report and opinion thereon by independent public accountants of national standing selected by the Company's Board of Directors.

(c) The Company will furnish each Investor, as soon as practicable after the end of the first, second and third quarterly accounting periods in each fiscal year of the Company, and in any event within forty-five (45) days thereafter, a consolidated balance sheet of the Company as of the end of each such quarterly period, and a consolidated statement of income and a consolidated statement of cash flows of the Company for such period and for the current fiscal year to date, prepared in accordance with generally accepted accounting principles, with the exception that no notes need be attached to such statements and year-end audit adjustments may not have been made.

(d) So long as an Investor (with its affiliates) shall own not less than three-hundred thousand (300,000) shares of Registrable Securities (as adjusted for stock splits and combinations) (a "Major Investor"), the Company will furnish each such Major Investor (i) at least thirty (30) days prior to the beginning of each fiscal year an annual budget and operating plans for such fiscal year (and as soon as available, any subsequent revisions thereto); and (ii) as soon as practicable after the end of each month, and in any event within twenty (20) days thereafter, a consolidated balance sheet of the Company as of the end of each such month, and a consolidated statement of income and a consolidated statement of cash flows of the Company for such month and for the current fiscal year to date, including a comparison to plan figures for such period, prepared in accordance with generally accepted accounting principles consistently applied, with the exception that no notes need be attached to such statements and year-end audit adjustments may not have been made.

3.2 INSPECTION RIGHTS. Each Investor shall have the right to visit and inspect any of the properties of the Company or any of its subsidiaries, and to discuss the affairs, finances and accounts of the Company or any of its subsidiaries with its officers, and to review such information as is reasonably requested all at such reasonable times and as often as may be reasonably requested; provided, however, that the Company shall not be obligated under this Section 3.2 with respect to a competitor of the Company or with respect to information which the Board of Directors determines in good faith is confidential and should not, therefore, be disclosed.

3.3 CONFIDENTIALITY OF RECORDS. Each Investor agrees to use, and to use its best efforts to insure that its authorized representatives use, the same degree of care as such Investor uses to protect its own confidential information to keep confidential any information furnished to it which the Company identifies as being confidential or proprietary (so long as such information is not in the public domain), except that such Investor may disclose such proprietary or confidential information to any partner, subsidiary or parent of such Investor for the purpose of

evaluating its investment in the Company as long as such partner, subsidiary or parent is advised of the confidentiality provisions of this Section 3.3.

3.4 RESERVATION OF COMMON STOCK. The Company will at all times reserve and keep available, solely for issuance and delivery upon the conversion of the Preferred Stock, all Common Stock issuable from time to time upon such conversion.

3.5 STOCK VESTING. Unless otherwise approved by the Board of Directors, all stock options and other stock equivalents issued after the date of this Agreement to employees, directors, consultants and other service providers shall be subject to vesting as follows: (i) twenty percent (20%) of such stock shall vest at the end of the first year following the earlier of the date of issuance or such person's services commencement date with the company, and (ii) eighty percent (80%) of such stock shall vest over the remaining four (4) years. With respect to any shares of stock purchased by any such person, the Company's repurchase option shall provide that upon such person's termination of employment or service with the Company, with or without cause, the Company or its assignee (to the extent permissible under applicable securities laws and other laws) shall have the option to purchase at cost any unvested shares of stock held by such person.

3.6 EXECUTIVE OFFICER COMPENSATION. The Board of Directors of the Company shall have the discretion to evaluate and modify the compensation of the Company's executive officers from time to time (including at the first meeting of the Board of Directors which occurs after the date hereof).

3.7 PROPRIETARY INFORMATION AND INVENTIONS AGREEMENT. The Company shall require all officers and employees to execute and deliver a Proprietary Information and Inventions Agreement in the form attached to the Purchase Agreement. The Company shall require all consultants to execute and deliver a consulting agreement containing confidentiality and assignment of inventions provisions similar to those included in the Proprietary Information and Inventions Agreement.

3.8 DIRECTORS' LIABILITY AND INDEMNIFICATION. The Company's Certificate of Incorporation and Bylaws shall provide (i) for elimination of the liability of directors to the maximum extent permitted by law and (ii) for indemnification of directors for acts on behalf of the Company to the maximum extent permitted by law.

3.9 REAL PROPERTY HOLDING CORPORATION. The Company covenants that it will operate in a manner such that it will not become a "United States real property holding corporation" ("USRPHC") as that term is defined in Section 897(c)(2) of the Internal Revenue Code of 1986, as amended, and the regulations thereunder ("FIRPTA"). The Company agrees to make determinations as to its status as a USRPHC, and will file statements concerning those determinations with the Internal Revenue Service, in the manner and at the times required under Reg. Section 1.897-2(h), or any supplementary or successor provision thereto. Within 30 days of a request from an Investor or any of its partners, the Company will inform the requesting party, in the manner set forth in Reg. Section 1.897-2(h)(1)(iv) or any supplementary or successor provision thereto, whether that party's interest in the Company constitutes a United States real property

interest (within the meaning of Internal Revenue Code Section 897(c)(1) and the regulations thereunder) and whether the Company has provided to the Internal Revenue Service all required notices as to its USRPHC status.

3.10 TERMINATION OF COVENANTS. All covenants of the Company contained in Section 3 of this Agreement shall expire and terminate as to each Investor on the effective date of the registration statement pertaining to a firmly underwritten public offering of shares of Common Stock of the Company at a price per share not less than $3.50 and for a total offering of not less than $15.0 million (before deduction of underwriters commissions and expenses) (a "Qualified IPO").

SECTION 4. RIGHTS OF FIRST REFUSAL

4.1 SUBSEQUENT OFFERINGS. Each Major Investor shall have a right of first refusal to purchase its pro rata share of all Equity Securities, as defined below, that the Company may, from time to time, propose to sell and issue after the date of this Agreement, other than the Equity Securities excluded by Section 4.6 hereof. Each Investor's pro rata share is equal to the ratio of (A) the number of shares of the Company's Common Stock (including all shares of Common Stock issued or issuable upon conversion of the Shares) of

which such Investor is deemed to be a holder immediately prior to the issuance of such Equity Securities to (B) the total number of shares of the Company's outstanding Common Stock (including all shares of Common Stock issued or issuable upon conversion of the Shares) immediately prior to the issuance of the Equity Securities. The term "Equity Securities" shall mean (i) any Common Stock, Preferred Stock or other security of the Company, (ii) any security convertible, with or without consideration, into any Common Stock, Preferred Stock or other security (including any option to purchase such a convertible security), (iii) any security carrying any warrant or right to subscribe to or purchase any Common Stock, Preferred Stock or other security, or (iv) any such warrant or right.

4.2 EXERCISE OF RIGHTS. If the Company proposes to issue any Equity Securities, it shall give each Major Investor written notice of its intention, describing the Equity Securities, the price and the terms and conditions upon which the Company proposes to issue the same. Each Major Investor shall have fifteen (15) days from the giving of such notice to agree to purchase its pro rata share of the Equity Securities for the price and upon the terms and conditions specified in the notice by giving written notice to the Company and stating therein the quantity of Equity Securities to be purchased. Notwithstanding the foregoing, the Company shall not be required to offer or sell such Equity Securities to any Investor who would cause the Company to be in violation of applicable federal securities laws by virtue of such offer or sale.

4.3 ISSUANCE OF EQUITY SECURITIES TO OTHER PERSONS. If not all of the Major Investors elect to purchase their pro rata share of the Equity Securities, then the Company shall promptly notify in writing the Major Investors who do so elect and shall offer such Major Investors the right to acquire such unsubscribed shares. The Major Investors shall have five (5) days after receipt of such notice to notify the Company of its election to purchase all or a portion thereof of the unsubscribed shares. If the Investors fail to exercise in full the rights of first

refusal, the Company shall have ninety (90) days thereafter to sell the Equity Securities in respect of which the Major Investors' rights were not exercised, at a price and upon general terms and conditions materially no more favorable to the purchasers thereof than specified in the Company's notice to the Major Investors pursuant to Section 4.2 hereof. If the Company has not sold such Equity Securities within ninety (90) days of the notice provided pursuant to Section 4.2, the Company shall not thereafter issue or sell any Equity Securities without first offering such securities to the Major Investors in the manner provided above.

4.4 TERMINATION OF RIGHTS OF FIRST REFUSAL. The rights of first refusal established by this Section 4 shall not apply to, and shall terminate upon the effective date of the registration statement pertaining to a Qualified IPO.

4.5 TRANSFER OF RIGHTS OF FIRST REFUSAL. The rights of first refusal of each Major Investor under this Section 4 may be transferred to the same parties, subject to the same restrictions as any transfer of registration rights pursuant to Section 2.10.

4.6 EXCLUDED SECURITIES. The rights of first refusal established by this Section 4 shall have no application to any of the following Equity Securities:

(a) up to an aggregate amount of 9,525,000 shares of Common Stock (and/or options, warrants or other Common Stock purchase rights issued pursuant to such options, warrants or other rights) issued or to be issued to employees, officers or directors of, or consultants or advisors to, the Company or any subsidiary, pursuant to stock purchase or stock option plans or other arrangements that are approved by the Board of Directors;

(b) stock issued pursuant to any rights or agreements outstanding as of the date of this Agreement, options and warrants outstanding as of the date of this Agreement; and stock issued pursuant to any such rights or agreements granted after the date of this Agreement, provided that the rights of first refusal established by this Section 4 applied with respect to the initial sale or grant by the Company of such rights or agreements;

(c) any Equity Securities issued for consideration other than cash pursuant to a merger, consolidation, acquisition or similar business combination;

(d) shares of Common Stock issued in connection with any stock split, stock dividend or recapitalization by the Company;

(e) shares of Common Stock issued upon conversion of the Shares;

(f) any Equity Securities issued pursuant to any equipment leasing arrangement, or debt financing from a bank or similar financial

institution;

(g) any Equity Securities that are issued by the Company pursuant to a registration statement filed under the Securities Act; and

(h) shares of the Company's Common Stock or Preferred Stock issued in connection with strategic transactions involving the Company and other entities, including (A) joint ventures, manufacturing, marketing or distribution arrangements or (B) technology transfer or development arrangements; provided that such strategic transactions and the issuance of shares therein, has been approved by the Company's Board of Directors.

SECTION 5. MISCELLANEOUS

5.1 GOVERNING LAW. This Agreement shall be governed by and construed under the laws of the State of California as applied to agreements among California residents entered into and to be performed entirely within California.

5.2 SURVIVAL. The representations, warranties, covenants, and agreements made herein shall survive any investigation made by any Holder and the closing of the transactions contemplated hereby. All statements as to factual matters contained in any certificate or other instrument delivered by or on behalf of the Company pursuant hereto in connection with the transactions contemplated hereby shall be deemed to be representations and warranties by the Company hereunder solely as of the date of such certificate or instrument.

5.3 SUCCESSORS AND ASSIGNS. Except as otherwise expressly provided herein, the provisions hereof shall inure to the benefit of, and be binding upon, the successors, assigns, heirs, executors, and administrators of the parties hereto and shall inure to the benefit of and be enforceable by each person who shall be a holder of Registrable Securities from time to time; provided, however, that prior to the receipt by the Company of adequate written notice of the transfer of any Registrable Securities specifying the full name and address of the transferee, the Company may deem and treat the person listed as the holder of such shares in its records as the absolute owner and holder of such shares for all purposes, including the payment of dividends or any redemption price.

5.4 ENTIRE AGREEMENT. This Agreement, the Exhibits and Schedules hereto, the Purchase Agreement and the other documents delivered pursuant thereto constitute the full and entire understanding and agreement between the parties with regard to the subjects hereof and no party shall be liable or bound to any other in any manner by any representations, warranties, covenants and agreements except as specifically set forth herein and therein.

5.5 SEVERABILITY. In case any provision of this Agreement shall be invalid, illegal, or unenforceable, the validity, legality, and enforceability of the remaining provisions shall not in any way be affected or impaired thereby.

5.6 AMENDMENT AND WAIVER.

(a) Except as otherwise expressly provided, this Agreement may be amended or modified only upon the written consent of the Company and the holders of at least two-thirds (66 2/3%) of the Registrable Securities.

(b) Except as otherwise expressly provided, the obligations of the Company and the rights of the Holders under this Agreement may be waived only with the written consent of the holders of at least two-thirds (66 2/3%) of the Registrable Securities.

(c) Notwithstanding the foregoing, this Agreement may be amended with only the written consent of the Company to include additional purchasers of Shares as "Investors," "Holders" and parties hereto.

5.7 DELAYS OR OMISSIONS. It is agreed that no delay or omission to exercise any right, power, or remedy accruing to any Holder, upon any breach, default or noncompliance of the Company under this Agreement shall impair any such right, power, or remedy, nor shall it be construed to be a waiver of any such breach, default or noncompliance, or any acquiescence therein, or of any similar breach, default or noncompliance thereafter occurring. It is further agreed that any waiver, permit, consent, or approval of any kind or character on any Holder's part of any breach, default or noncompliance under this Agreement or any waiver on such Holder's part of any provisions or conditions of this Agreement must be in writing and shall be effective only to the extent specifically set forth in such writing. All remedies, either under this

Agreement, by law, or otherwise afforded to Holders, shall be cumulative and not alternative.

5.8 NOTICES. All notices required or permitted hereunder shall be in writing and shall be deemed effectively given: (i) upon personal delivery to the party to be notified, (ii) when sent by confirmed telex or facsimile if sent during normal business hours of the recipient; if not, then on the next business day, (iii) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (iv) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent to the party to be notified at the address as set forth on the signature pages hereof or Schedule A hereto or at such other address as such party may designate by ten (10) days advance written notice to the other parties hereto.

5.9 ATTORNEYS' FEES. In the event that any dispute among the parties to this Agreement should result in litigation, the prevailing party in such dispute shall be entitled to recover from the losing party all fees, costs and expenses of enforcing any right of such prevailing party under or with respect to this Agreement, including without limitation, such reasonable fees and expenses of attorneys and accountants, which shall include, without limitation, all fees, costs and expenses of appeals.

5.10 TITLES AND SUBTITLES. The titles of the sections and subsections of this Agreement are for convenience of reference only and are not to be considered in construing this Agreement.

5.11 COUNTERPARTS. This Agreement may be executed in any number of counterparts, each of which shall be an original, but all of which together shall constitute one instrument.

Agreed and executed by:

RIGEL PHARMACEUTICALS

By: _____

Name: _____

Title: _____

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

FRAZIER HEALTHCARE II, L.P.

By: _____

Name: _____

Title: _____

FRAZIER & COMPANY, INC.

By: _____

Name: _____

Title: _____

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

LOMBARD, ODIER & CIE

By: _____

Name: _____

Title: _____

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

ALTA CALIFORNIA PARTNERS, L.P.
By: Alta California Management Partners, L.P.

By: _____
General Partner

ALTA EMBARCADERO PARTNERS, LLC

By: _____
Member

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

FORTUNE MAKER CORPORATION

By: _____

Name: _____

Title: _____

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

JOHNSON & JOHNSON DEVELOPMENT CORPORATION

By: _____

Name: _____

Title: _____

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

NOVARTIS PHARMA AG

By: _____

Name: _____

Title: _____

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

PFIZER, INC.

By: _____

Name: _____

Title: _____

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

CMEA LIFE SCIENCES FUND, L.P.

By: _____

Name: _____

Title: _____

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

AURORA BIOSCIENCES CORPORATION

By: _____

Name: _____

Title: _____

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

CB CAPITAL INVESTORS, L.P.

By: Chase Capital Partners

Its: Manager

Name:

Title:

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

SUMMIT BANK & TRUST CO.

By:

Name:

Title:

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

R.A. INVESTMENT GROUP

By:

Name:

Title:

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

QUANTUM PARTNERS LDC

By:

Name:

Title:

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

GC & H INVESTMENTS

By:

Name:

Title:

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

Thomas Volpe

AMENDED AND RESTATED INVESTOR RIGHTS AGREEMENT
SIGNATURE PAGE

RIGEL PHARMACEUTICALS, INC.
SERIES E PREFERRED STOCK FINANCING
SCHEDULE OF PURCHASERS
FIRST CLOSING-FEBRUARY 3, 2000

<TABLE>
<CAPTION>

NAME AND ADDRESS	INVESTMENT AMOUNT	NUMBER OF SHARES
<S>	<C>	<C>
Alta California Partners, L.P. One Embarcadero Center, Suite 4050 San Francisco, CA 94111	$ 977,664	162,944
Alta Embarcadero Partners, LLC One Embarcadero Center, Suite 4050 San Francisco, CA 94111	$ 22,338	3,723
Fortune Maker Corporation 11/F King Fook Building 30-32 Des Voeux Road Central HONG KONG	300,000	50,000
Frazier Healthcare II, L.P. Two Union Square 601 Union Street, Suite 3300 Seattle, WA 98101	750,000	125,000
CMEA Life Sciences Fund 235 Montgomery Street, Suite 920 San Francisco, CA 94104	1,000,000	166,666
CB Capital Investors c/o Chase Capital Partners Partners 380 Madison Avenue 12th Floor New York, NY 10017	5,000,000	833,333
Pritzker Entities		
Cynthia J. Cohn	99,996	16,666
Hannah S. & Samuel A. Cohn Memorial Foundation	99,996	16,666
R.A. Investments Group c/o Diversified Financial Management Group 200 West Madison Street Suite 3800 Chicago, IL 50606	800,000	133,333
Quantum Partners LDC 888 Seventh Avenue New York, NY 10106	2,000,000	333,333

Johnson & Johnson Development Corporation One Johnson & Johnson Plaza New Brunswick, NJ 08933	1,000,000	166,666

Schedule A-1

Lombard, Odier & Cie Toedistrasse 36 - Ch 8027 Zurich Switzerland	3,000,000	500,000
Aurora Biosciences Corporation 11010 Torreyana Road San Diego, CA 92121	Transfer of Technology	50,000
TOTAL	$15,049,994	2,558,330

</TABLE>

Schedule A-2

RIGEL PHARMACEUTICALS, INC.
SERIES E PREFERRED STOCK FINANCING
SCHEDULE OF PURCHASERS
SECOND CLOSING - AUGUST 31, 2000

<TABLE>
<CAPTION>

NAME AND ADDRESS	INVESTMENT AMOUNT	NUMBER OF SHARES
<S>	<C>	<C>
Thomas Volpe The Prudential Volpe Technology Group One Maritime Plaza Fifth Floor San Francisco, CA 94111	$199,998	33,333
TOTAL	$199,998	33,333

</TABLE>

Schedule A-3

THIS WARRANT HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "1933 ACT"), OR ANY APPLICABLE STATE SECURITIES LAWS, AND MAY NOT BE SOLD OR TRANSFERRED UNLESS SUCH SALE OR TRANSFER IS IN ACCORDANCE WITH THE REGISTRATION REQUIREMENTS OF SUCH ACT AND APPLICABLE LAWS OR. SOME OTHER EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF SUCH ACT AND APPLICABLE LAWS IS AVAILABLE WITH RESPECT THERETO.

COMMON STOCK PURCHASE WARRANT

Warrant No. CS- Number of Shares: Common Stock

RIGEL PHARMACEUTICALS, INC.

1. ISSUANCE. This Warrant is issued to , by RIGEL PHARMACEUTICALS, INC., a Delaware corporation (hereinafter with its successors called the "COMPANY").

2. PURCHASE PRICE; NUMBER OF SHARES. The registered holder of this Warrant (the "HOLDER"), commencing on the date hereof, is entitled upon surrender of this Warrant with the subscription form annexed hereto duly executed, at the principal office of the Company, to purchase from the Company the following securities (collectively, the "SHARES") at a price per share of $1.14 (the "PURCHASE PRICE"), ( ) fully paid and nonassessable shares of Common Stock, $.001 par value, of the Company (the "COMMON STOCK"). Until such time as this Warrant is exercised in full or expires, the Purchase Price and the securities issuable upon exercise of this Warrant are subject to adjustment as hereinafter provided. The person or persons on whose name or names any certificate representing shares of Common Stock is issued hereunder shall be deemed to have become the holder of record of the shares represented thereby as at the close of business on the date this Warrant is exercised with respect to such shares, whether or not the transfer books of the Company shall be closed.

3. PAYMENT OF PURCHASE PRICE. The Purchase Price may be paid (i) in cash or by Check, (ii) by the surrender by the Holder to the Company of any promissory notes or other obligations issued by the Company, with all such notes and obligations so surrendered being credited against the Purchase Price in an amount equal to the principal amount thereof plus accrued interest to the date of surrender, or (iii) by any combination of the foregoing.

4. NET ISSUE ELECTION. The Holder may elect to receive, without the payment by the Holder of any additional consideration, shares of Common Stock equal to the value of this Warrant or any portion hereof by the surrender of this Warrant or such portion to the Company, with the net issue election notice annexed hereto duly executed, at the principal office of the Company. Thereupon, the Company shall issue to the Holder such number of fully paid and nonassessable shares of Common Stock as is computed using the following formula:

$$X = \frac{Y\,(A-B)}{A}$$

where: X = the number of shares of Common Stock to be issued to the Holder pursuant to this Section 4.

Y = the number of shares of Common Stock covered by this Warrant in respect of which the net issue election is made pursuant to this Section 4.

A = the Fair Market Value (defined below) of one share of Common Stock, as determined at the time the net issue election is made pursuant to this Section 4.

B = the Purchase Price in effect under this Warrant at the time the net issue election is made pursuant to this Section 4.

"Fair Market Value" of a share of Common Stock as of a particular date (the "Determination Date") shall mean:

(a) If the net issue election is made in connection with and contingent upon the closing of the sale of the Company's Common Stock to the public in a public offering pursuant to a Registration Statement under the Act (a "Public Offering"), and if the Company's Registration Statement relating to such Public Offering ("Registration Statement") has been declared effective by the SEC, then the initial "Price to Public" specified in the

final prospectus with respect to such offering multiplied by the number of shares of Common Stock into which each share of Preferred Stock is then convertible.

(b) If the net issue election is not made in connection with and contingent upon a Public Offering, then as follows:

(i) If traded on a securities exchange or the Nasdaq National Market, the fair market value of the Common Stock shall be deemed to be the average of the closing or last reported sale prices of the Common Stock on such exchange or market over the 30-day period ending five business days prior to the Determination Date (or, if traded on a securities exchange or the Nasdaq National Market for less than 35 days as of the Determination Date, over the period beginning on the date of the Public Offering and ending five business days prior to the Determination Date);

(ii) If otherwise traded in an over-the-counter market, the fair market value of the Common Stock shall be deemed to be the average of the closing ask prices of the Common Stock over the 30-day period ending five business days prior to the Determination Date; and

(iii) If there is no public market for the Common Stock, then fair market value shall be determined in good faith by the Company's Board of Directors.

5. PARTIAL EXERCISE. This Warrant may be exercised in part, and the Holder shall be entitled to receive a new warrant, which shall be dated as of the date of this Warrant, covering the number of shares in respect of which this Warrant shall not have been exercised.

6. FRACTIONAL SHARES. In no event shall any fractional share of Common Stock be issued upon any exercise of this Warrant. If, upon exercise of this Warrant as an entirety, the Holder would, except as provided in this Section 6, be entitled to receive a fractional share of Common Stock, then the Company shall pay in lieu thereof, the Fair Market Value of such fractional share in cash.

7. EXPIRATION DATE; AUTOMATIC EXERCISE. Except as otherwise set forth in Section 10, this Warrant shall expire on the earlier of (i) the close of business on June 1, 2008 and (ii) seven years after the closing of the initial public offering of the Company's Common Stock pursuant to a registration statement under the Securities Act of 1933, as amended, and shall be void thereafter.

8. RESERVED SHARES; VALID ISSUANCE. The Company covenants that it will at all times from and after the date hereof reserve and keep available such number of its authorized shares of Common Stock, $.001 par value, of the Company (the "COMMON STOCK"), free from all preemptive or similar rights therein, as will be sufficient to permit, respectively, the exercise of this Warrant in full and the conversion into shares of Common Stock upon such exercise. The Company further covenants that such shares as may be issued pursuant to such exercise and/or conversion will, upon issuance, be duly and validly issued, fully paid and nonassessable and free from all taxes, liens and charges with respect to the issuance thereof.

9. STOCK SPLITS AND DIVIDENDS. If after the date hereof the Company shall subdivide the Common Stock, by split-up or otherwise, or combine the Common Stock. or issue additional shares of Common Stock in payment of a stock dividend on the Common Stock, the number of shares of Common Stock issuable on the exercise of this Warrant shall forthwith be proportionately increased in the case of a subdivision or stock dividend, or proportionately decreased in the case of a combination, and the Purchase Price shall forthwith be proportionately decreased in the case of a subdivision or stock dividend, or proportionately increased in the case of a combination.

10. MERGERS AND RECLASSIFICATIONS. If after the date hereof the Company shall enter into any Reorganization (as hereinafter defined), then, as a condition of such Reorganization, lawful provisions shall be made, and duly executed documents evidencing the same from the Company or its successor shall be delivered to the Holder, so that the Holder shall thereafter have the right to purchase, at a total price not to exceed that payable upon the exercise of this Warrant in full, the kind and amount of shares of stock and other securities and property receivable upon such Reorganization by a holder of the number of shares of Common Stock which might have been purchased by the Holder immediately prior to such Reorganization, and in any such case appropriate provisions shall be made with respect to the rights and interest of the Holder to the end that the provisions hereof (including without limitation, provisions for the adjustment of the Purchase Price and the number of shares issuable hereunder and the provisions relating to the net issue election) shall thereafter be applicable in relation to any shares of stock or other securities and property thereafter deliverable upon exercise hereof. For the purposes of this Section 10, the term "Reorganization" shall

include without limitation any reclassification, capital reorganization or change of the Common Stock (other than as a result of a subdivision,

combination or stock dividend provided for in Section 9 hereof), or any consolidation of the Company with, or merger of the Company into, another corporation or other business organization (other than a merger in which the Company is the surviving corporation and which does not result in any reclassification or change of the outstanding Common Stock), or any sale or conveyance to another corporation or other business organization of all or substantially all of the assets of the Company.

Notwithstanding the term of this Warrant fixed pursuant to Section 7 above and the provisions of this Section 10, the right to purchase Common Stock as granted herein shall expire, to the extent not previously exercised, immediately upon the closing of a merger or consolidation of the Company with or into another corporation when the Company is not the surviving corporation (other than a merger or consolidation for the principal purpose of changing the domicile of the Company), and provided that any securities received in such merger or consolidation are publicly traded or the sale of all or substantially all of the Company's capital stock, properties and assets to any other person, in each case where the stockholders of the Company immediately prior to such merger, consolidation or sale of assets own (directly or indirectly) less than 50% of the voting securities of the surviving entity or purchaser of assets in such transaction (collectively, a "Merger"), except to the extent assumed by the successor corporation (or parent thereof) in connection with such Merger. In the event that any outstanding warrants to purchase equity securities of the Company are assumed, this Warrant shall also be similarly assumed.

The Company shall notify the Holder at least fifteen (15) calendar days prior to any proposed Merger, and if the Company fails to deliver such notice, then notwithstanding anything to the contrary in this Warrant, the rights to purchase the Company's Common Stock (or the shares of stock and other securities and property receivable upon such Merger by a holder of Common Stock (the "OTHER CONSIDERATION")) shall not expire. The Holder may exercise the Warrant contingent upon the closing of the Merger. If the Merger does not close within 60 days after notice, any contingent exercise shall be void.

11. CERTIFICATE OF ADJUSTMENT. Whenever the Purchase Price is adjusted, as herein provided, the Company shall promptly deliver to the Holder a certificate of the Company's chief financial officer setting forth the Purchase Price after such adjustment and setting forth a brief statement of the facts requiring such adjustment.

12. NOTICES OF RECORD DATE, ETC. In the event of:

(a) any taking by the Company of a record of the holders of any class of securities for the purpose of determining the holders thereof who are entitled to receive any dividend or other distribution, or any right to subscribe for, purchase, sell or otherwise acquire or dispose of any shares of stock of any class or any other securities or property, or to receive any other right;

(b) any reclassification of the capital stock of the Company, capital reorganization of the Company, consolidation or merger involving the Company, or sale or conveyance of all or substantially all of its assets; or

(c) any voluntary or involuntary dissolution, liquidation or winding-up of the Company;

then in each such event the Company will provide or cause to be provided to the Holder a written notice thereof. Such notice shall be provided at least fifteen (15) calendar days prior to the date specified in such notice on which any such action is to be taken.

13. CORPORATE INFORMATION. As a courtesy to Holder and in order to enable Holder to make informed decisions regarding the possible exercise of this Warrant from time to time, the Company agrees, upon written request by Holder to the chief financial officer of the Company from time to time (but not more often than twice in any 12-month period), to provide to Holder copies of the following documents within a reasonable time after such request (but in all events only to the extent that, and no sooner than the time that, such documents have been distributed or made available to all the Company's stockholders): (i) the Company's most recent audited annual financial statements or, if audited statements are not available, then the Company's unaudited annual financial statements as of the end of the Company's most recently ended fiscal year; (ii) unaudited quarterly financial statements for each quarter of the Company's fiscal year since the date of the annual

financial statements delivered pursuant to clause (i) above; and (iii) any other reports, proxy statements or notices distributed to holders of the Company's Common Stock within the last twelve (12) months preceding such request (or within the period since the last such request by Holder. whichever is shorter). Notwithstanding the preceding sentence, when the Company has outstanding a class of publicly-traded securities or is for any other reason a reporting company under the Securities Exchange Act of 1934, the rights under this Section 13 shall terminate.

14. REPRESENTATIONS, WARRANTIES AND COVENANTS. This Warrant is issued and delivered by the Company and accepted by each Holder on the basis of the following representations, warranties and covenants made by the Company:

(a) The Company has all necessary authority to issue, execute and deliver this Warrant and to perform its obligations hereunder. This Warrant has been duly authorized issued, executed and delivered by the Company and is the valid and binding obligation of the Company, enforceable in accordance with its terms, except as enforceability may be limited by bankruptcy, insolvency, reorganization or other similar laws of general application affecting the enforcement of Holders rights or by general equity principals or public policy concerns.

(b) The shares of Common Stock issuable upon the exercise of this Warrant have been duly authorized and reserved for issuance by the Company and, when issued in accordance with the terms hereof, will be validly issued, fully paid and nonassessable.

(c) The issuance, execution and delivery of this Warrant do not, and the issuance of the shares of Common Stock upon the exercise of this Warrant in accordance with the terms hereof will not, (i) violate or contravene the Company's Certificate of Incorporation or by-laws, or any law, statute, regulation, rule, judgment or order applicable to the Company, (ii) violate, contravene or result in a breach or default under any material contract, agreement or instrument to which the Company is a party or by which the Company or any of its assets are

bound or (iii) require the consent or approval of or the filing of any notice or registration with any person or entity.

15. AMENDMENT AND WAIVER. The terms of this Warrant may be amended, modified or waived only with the written consent of the party against which enforcement of the same is sought.

16. REPRESENTATIONS AND COVENANTS OF THE HOLDER. This Common Stock Purchase Warrant has been entered into by the Company in reliance upon the following representations and covenants of the Holder, which by its execution hereof the Holder hereby confirms:

(a) INVESTMENT PURPOSE. The right to acquire Common Stock or the Common Stock issuable upon exercise of the Holder's rights contained herein will be acquired for investment and not with a view to the sale or distribution of any part thereof, and the Holder has no present intention of selling or engaging in any public distribution of the same except pursuant to a registration or exemption.

(b) ACCREDITED INVESTOR. Holder is an "accredited investor" within the meaning of the Securities and Exchange Rule 501 of Regulation D, as presently in effect.

(c) PRIVATE ISSUE. The Holder understands (i) that the Common Stock issuable upon exercise of the Holder's rights contained herein is not registered under the 1933 Act or qualified under applicable state securities laws on the ground that the issuance contemplated by this Warrant will be exempt from the registration and qualifications requirements thereof, and (ii) that the Company's reliance on such exemption is predicated on the representations set forth in this Section 16.

(d) FINANCIAL RISK. The Holder has such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of its investment and has the ability to bear the economic risks of its investment.

17. NOTICES, TRANSFERS, ETC.

(a) Any notice or written communication required or permitted to be given to the Holder may be given by certified mall or delivered to the Holder at the address most recently provided by the Holder to the Company.

(b) Subject to compliance with applicable federal and state securities laws, this Warrant may be transferred by the Holder with respect to any or all of the shares purchasable hereunder. Upon surrender of this Warrant to the Company, together with the assignment notice annexed hereto

duly executed, for transfer of this Warrant as an entirety by the Holder, the Company shall issue a new warrant of the same denomination to the assignee. Upon surrender of this Warrant to the Company, together with the assignment hereof properly endorsed, by the Holder for transfer with respect to a portion of the shares of Preferred Stock purchasable hereunder, the Company shall issue a new warrant to the assignee, in such denomination as shall

be requested by the Holder hereof, and shall issue to such Holder a new warrant covering the number of shares in respect of which this Warrant shall not have been transferred.

(c) In case this Warrant shall be mutilated, lost, stolen or destroyed, the Company shall issue a new warrant of like tenor and denomination and deliver the same (i) in exchange and substitution for and upon surrender and cancellation of any mutilated Warrant, or (ii) in lieu of any Warrant lost, stolen or destroyed, upon receipt of an affidavit of the Holder or other evidence reasonably satisfactory to the Company of the loss, theft or destruction of such Warrant and an indemnification of loss by the Holder in favor of the Company.

18. NO IMPAIRMENT. The Company will not, by amendment of its Certificate or through any reclassification, capital reorganization, consolidation, merger, sale or conveyance of assets, dissolution, liquidation, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance of performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such action as may be necessary or appropriate in order to protect the rights of the Holder.

19. GOVERNING LAW. The provisions and terms of this Warrant shall be governed by and construed in accordance with the internal laws of the State of California.

20. SUCCESSORS AND ASSIGNS. This Warrant shall be binding upon the Company's successors and assigns and shall inure to the benefit of the Holder's successors, legal representatives and permitted assigns.

21. BUSINESS DAYS. If the last or appointed day for the taking of any action required or the expiration of any rights granted herein shall be a Saturday or Sunday or a legal holiday in California, then such action may be taken or right may be exercised on the next succeeding day which is not a Saturday or Sunday or such a legal holiday.

DATED: June 2, 1998 RIGEL PHARMACEUTICALS, INC.

By: /s/ James M Gower

Name: James Gower

Title: President

SUBSCRIPTION

To:_____ Date:_____

The undersigned hereby subscribes for _____ shares of Preferred Stock covered by this Warrant. The certificate(s) for such shares shall be issued in the name of the undersigned or as otherwise indicated below:

_____
Signature

_____
Name for Registration

_____
Mailing Address

NET ISSUE ELECTION NOTICE

To:_____ Date:_____

The undersigned hereby elects under Section 4 to surrender the right to purchase _____ shares of Preferred Stock pursuant to this Warrant. The certificate(s) for such shares issuable upon such net issue election

shall be issued in the name of the undersigned or as otherwise indicated below:

_____
Signature

_____
Name for Registration

_____
Mailing Address

ASSIGNMENT

For value received _____ hereby sells, assigns and transfers unto _____

_____
[Please print or typewrite name and address of Assignee]

_____

the within Warrant, and does hereby irrevocably constitute and appoint _____ its attorney to transfer the within Warrant on the books of the within named Company with full power of substitution on the premises.

DATED:_____ _____

IN THE PRESENCE OF:

_____

Exhibit 4.4

THIS WARRANT HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "1933 ACT"), OR ANY APPLICABLE STATE SECURITIES LAWS. AND MAY NOT BE SOLD OR TRANSFERRED UNLESS SUCH SALE OR TRANSFER IS IN ACCORDANCE WITH THE REGISTRATION REQUIREMENTS OF SUCH ACT AND APPLICABLE LAWS OR SOME OTHER EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF SUCH ACT AND APPLICABLE LAWS IS AVAILABLE WITH RESPECT THERETO.

PREFERRED STOCK PURCHASE WARRANT

Warrant No. PSB-1 — Number of Shares 175,000 Series B Preferred Stock

RIGEL PHARMACEUTICALS, INC.

Void after April 30, 2004

1. ISSUANCE. This Warrant is issued to LIGHTHOUSE CAPITAL PARTNERS II, L.P. by RIGEL PHARMACEUTICALS, INC., a Delaware corporation (hereinafter with its successors called the "COMPANY").

2. PURCHASE PRICE; NUMBER OF SHARES. The registered holder of this Warrant (the "HOLDER"), commencing on the date hereof, is entitled upon surrender of this Warrant with the subscription form annexed hereto duly executed, at the principal office of the Company, to purchase from the Company the following securities (collectively, the "SHARES") at a price per share of $0.80 (the "PURCHASE PRICE"), 175,000 fully paid and nonassessable shares of Series B Preferred Stock, $.001 par value, of the Company (the "PREFERRED STOCK"). Until such time as this Warrant is exercised in full or expires, the Purchase Price and the securities issuable upon exercise of this Warrant are subject to adjustment as hereinafter provided. The person or persons on whose name or names any certificate representing shares of Preferred Stock is issued hereunder shall be deemed to have become the holder of record of the shares represented thereby as at the close of business on the date this Warrant is exercised with respect to such shares, whether or not the transfer books of the Company shall be closed.

3. PAYMENT OF PURCHASE PRICE. The Purchase Price may be paid (i) in cash or by check, (ii) by the surrender by the Holder to the Company of any promissory notes or other obligations issued by the Company, with all such notes and obligations so surrendered being credited against the Purchase Price in an amount equal to the principal amount thereof plus accrued interest to the date of surrender, or (iii) by any combination of the foregoing.

4. NET ISSUE ELECTION. The Holder may elect to receive, without the payment by the Holder of any additional consideration, shares of Preferred Stock equal to the value of this Warrant or any portion hereof by the surrender of this Warrant or such portion to the Company, with the net issue election notice annexed hereto duly executed, at the principal office of the Company. Thereupon, the Company shall issue to the Holder such number of fully paid and nonassessable shares of Preferred Stock as is computed using the following formula:

$$X = \frac{Y\,(A-B)}{A}$$

where: X = the number of shares of Preferred Stock to be issued to the Holder pursuant to this SECTION 4.

Y = the number of shares of Preferred Stock covered by this Warrant in respect of which the net issue election is made pursuant to this SECTION 4.

A = the Fair Market Value (defined below) of one share of Preferred Stock, as determined at the time the net issue election is made pursuant to this SECTION 4.

B = the Purchase Price in effect under this Warrant at the time the net issue election is made pursuant to this SECTION 4.

"Fair Market Value" of a share of Preferred Stock (or Common Stock if the Preferred Stock has been automatically converted into Common Stock) as of a

particular date (the "Determination Date") shall mean:

(i) If the net issue election is made in connection with and contingent upon the closing of the sale of the Company's Common Stock to the public in a public offering pursuant to a Registration Statement under the Act (a "Public Offering"), and if the Company's Registration Statement relating to such Public Offering ("Registration Statement") has been declared effective by the SEC, then the initial "Price to Public" specified in the final prospectus with respect to such offering multiplied by the number of shares of Common Stock into which each share of Preferred Stock is then convertible.

(ii) If the net issue election is not made in connection with and contingent upon a Public Offering, then as follows:

(A) If traded on a securities exchange or the Nasdaq National Market, the fair market value of the Common Stock shall be deemed to be the average of the closing or last reported sale prices of the Common Stock on such exchange or market over the 30-day period ending five business days prior to the Determination Date, and the fair market value of the Preferred Stock shall be deemed to be such fair market value of the Common Stock multiplied by the number of shares of Common Stock into which each share of Preferred Stock is then convertible;

(B) If otherwise traded in an over-the-counter market, the fair market value of the Common Stock shall be deemed to be the average of the closing ask prices of the Common Stock over the 30-day period ending five business days prior to the Determination Date, and the fair market value of the Preferred Stock shall be deemed to be such fair market value of the Common Stock multiplied by the number of shares of Common Stock into which each share of Preferred Stock is then convertible; and

(C) If there is no public market for the Common Stock, then fair market value shall be determined in good faith by the Company's Board of Directors.

5. PARTIAL EXERCISE. This Warrant may be exercised in part, and the Holder shall be entitled to receive a new warrant, which shall be dated as of the date of this Warrant, covering the number of shares in respect of which this Warrant shall not have been exercised.

6. FRACTIONAL SHARES. In no event shall any fractional share of Preferred Stock be issued upon any exercise of this Warrant. If, upon exercise of this Warrant as an entirety, the Holder would, except as provided in this SECTION 6, be entitled to receive a fractional share of Preferred Stock, then the Company shall pay in lieu thereof, the Fair Market Value of such fractional share in cash.

7. EXPIRATION DATE; AUTOMATIC EXERCISE. Except as otherwise set forth in SECTION 11, this Warrant shall expire at the close of business on April 30, 2004 and shall be void thereafter. Notwithstanding the foregoing, this Warrant shall automatically be deemed to be exercised in full pursuant to the provisions of SECTION 4 hereof, without

any further action on behalf of the Holder, immediately prior to the time this Warrant would otherwise expire pursuant to the preceding sentence or pursuant to SECTION 11.

8. RESERVED SHARES; VALID ISSUANCE. The Company covenants that it will at all times from and after the date hereof reserve and keep available such number of its authorized shares of Preferred Stock and Common Stock, $.001 par value, of the Company (the "COMMON STOCK"), free from all preemptive or similar rights therein, as will be sufficient to permit, respectively, the exercise of this Warrant in full and the conversion into shares of Common Stock of all shares of Preferred Stock receivable upon such exercise. The Company further covenants that such shares as may be issued pursuant to such exercise and/or conversion will, upon issuance, be duly and validly issued, fully paid and nonassessable and free from all taxes, liens and charges with respect to the issuance thereof.

9. STOCK SPLITS AND DIVIDENDS. If after the date hereof the Company shall subdivide the Preferred Stock, by split-up or otherwise, or combine the Preferred Stock, or issue additional shares of Preferred Stock in payment of a stock dividend on the Preferred Stock, the number of shares of Preferred Stock issuable on the exercise of this Warrant shall forthwith be proportionately increased in the case of a subdivision or stock dividend, or proportionately decreased in the case of a combination, and the Purchase Price shall forthwith be proportionately decreased in the case of a subdivision or stock dividend, or

proportionately increased in the case of a combination.

10. ADJUSTMENTS FOR DILUTING ISSUANCES. The other antidilution rights applicable to the Preferred Stock and the Common Stock of the Company are set forth in the Amended and Restated Certificate of Incorporation, as amended from time to time (the "Articles"), a true and complete copy in its current form which is attached hereto as EXHIBIT A. Such rights shall not be restated, amended or modified in any manner which effects the Holder differently than the holders of Series B Preferred without such Holder's prior written consent. The Company shall promptly provide the Holder hereof with any restatement, amendment or modification to the Articles promptly after the same has been made.

11. MERGERS AND RECLASSIFICATIONS. If after the date hereof the Company shall enter into any Reorganization (as hereinafter defined), then, as a condition of such Reorganization, lawful provisions shall be made, and duly executed documents evidencing the same from the Company or its successor shall be delivered to the Holder, so that the Holder shall thereafter have the right to purchase, at a total price not to exceed that payable upon the exercise of this Warrant in full, the kind and amount of shares of stock and other securities and property receivable upon such Reorganization by a holder of the number of shares of Preferred Stock which might have been purchased by the Holder immediately prior to such Reorganization, and in any such case appropriate provisions shall be made with respect to the rights and interest of the Holder to the end that the provisions hereof (including without limitation, provisions for the adjustment of the Purchase Price and the number of shares issuable hereunder and the provisions relating to the net issue election) shall thereafter be applicable in relation to any shares of stock or other securities and property thereafter deliverable upon exercise hereof. For the purposes of this SECTION 11, the term "REORGANIZATION" shall include without limitation any reclassification, capital reorganization or change of the Preferred Stock (other than as a result of a subdivision, combination or stock dividend provided for in SECTION 9 hereof), or any consolidation of the Company with, or merger of the Company into, another corporation or other business organization (other than a merger in which the Company is the surviving corporation and which does not result in any reclassification or change of the outstanding Preferred Stock), or any sale or conveyance to another corporation or other business organization of all or substantially all of the assets of the Company.

Notwithstanding the term of this Warrant fixed pursuant to SECTION 7 above and the provisions of this SECTION 11, the right to purchase Preferred Stock as granted herein shall expire, to the extent not previously exercised, immediately upon the closing of a merger or consolidation of the Company with or into another corporation when the Company is not the surviving corporation (other than a merger or consolidation for the principal purpose of changing the domicile of the Company), or the sale of all or substantially all of the Company's capital stock, properties and assets to any other person, in each case where the stockholders of the Company immediately prior to such merger, consolidation or sale of assets own (directly or indirectly) less than 50% of the voting securities of the surviving entity or purchaser of assets in such transaction (collectively, a "Merger"), except to the extent assumed by the successor corporation (or parent thereof) in connection with such Merger. In the event that any outstanding warrants to purchase equity securities of the Company are assumed, this Warrant shall also be similarly assumed.

The Company shall notify the Holder within twenty (20) days of any proposed Merger, and if the Company fails to deliver such notice, then notwithstanding anything to the contrary in this Warrant, the rights to purchase the Company's Preferred Stock (or the shares of stock and other securities and property receivable upon such Merger by a holder of Preferred Stock (the "OTHER CONSIDERATION")) shall not expire. The Holder may exercise the Warrant contingent upon the closing of the Merger. If the Merger does not close within 60 days after notice, any contingent exercise shall be void.

12. CERTIFICATE OF ADJUSTMENT. Whenever the Purchase Price is adjusted, as herein provided, the Company shall promptly deliver to the Holder a certificate of the Company's chief financial officer setting forth the Purchase Price after such adjustment and setting forth a brief statement of the facts requiring such adjustment.

13. NOTICES OF RECORD DATE, ETC. In the event of:

(a) any taking by the Company of a record of the holders of any class of securities for the purpose of determining the holders thereof who are entitled to receive any dividend or other distribution, or any right to subscribe for, purchase, sell or otherwise acquire or dispose of any shares of stock of any class or any other securities or property, or to receive any other right;

(b) any reclassification of the capital stock of the Company, capital reorganization of the Company, consolidation or merger involving the Company, or sale or conveyance of all or substantially all of its assets; or

(c) any voluntary or involuntary dissolution, liquidation or winding-up of the Company;

then in each such event the Company will provide or cause to be provided to the Holder a written notice thereof. Such notice shall be provided at least twenty (20) business days prior to the date specified in such notice on which any such action is to be taken.

14. REPRESENTATIONS, WARRANTIES AND COVENANTS. This Warrant is issued and delivered by the Company and accepted by each Holder on the basis of the following representations, warranties and covenants made by the Company:

A. The Company has all necessary authority to issue, execute and deliver this Warrant and to perform its obligations hereunder. This Warrant has been duly authorized issued, executed and delivered by the Company and is the valid and binding obligation of the Company, enforceable in accordance with its terms, except as enforceability may be limited by bankruptcy, insolvency, reorganization or other similar laws of general application affecting the enforcement of Holders rights or by general equity principals or public policy concerns.

B. The shares of Preferred Stock issuable upon the exercise of this Warrant have been duly authorized and reserved for issuance by the Company and, when issued in accordance with the terms hereof, will be validly issued, fully paid and nonassessable.

C. The issuance, execution and delivery of this Warrant do not, and the issuance of the shares of Preferred Stock upon the exercise of this Warrant in accordance with the terms hereof will not, (i) violate or contravene the Company's Articles or by-laws, or any law, statute, regulation, rule, judgment or order applicable to the Company, (ii) violate, contravene or result in a breach or default under any material contract, agreement or instrument to which the Company is a party or by which the Company or any of its assets are bound or (iii) require the consent or approval of or the filing of any notice or registration with any person or entity.

D. So long as this Warrant has not terminated, Holder shall be entitled to receive such financial and other information as the Holder would be entitled to receive under the Series B Preferred Stock Purchase Agreement if Holder were a holder of that number of shares issuable upon full exercise of this Warrant.

E. As of the date hereof, the authorized capital stock of the Company consists of (i) 20,000,000 shares of Common Stock, of which 2,510,000 shares are issued and outstanding and 175,000 shares are reserved for

issuance upon the exercise of this Warrant and the conversion of the Preferred Stock, (ii) 665,000 shares of Series A Preferred Stock, of which 665,000 are issued and outstanding shares, and (iii) 7,675,000 shares of Series B Preferred Stock, of which 7,500,000 are issued and outstanding shares and 175,000 shares are reserved for issuance upon the exercise of this Warrant. Attached hereto as EXHIBIT B is a capitalization table summarizing the capitalization of the Company.

15. REGISTRATION RIGHTS. The Company grants to the Holder registration rights contained in SECTIONS 2.2, 2.3 and 2.4 of the Company's Investor Rights Agreement dated as of January 17, 1997 (the "INVESTOR RIGHTS AGREEMENT"), so that (i) the shares of Common Stock issuable upon conversion of the shares of Preferred Stock issuable upon exercise of this Warrant shall be "Registrable Securities," and (ii) the Holder shall be a "Holder" and "Investor" for all purposes of such Investor Rights Agreement.

16. AMENDMENT. The terms of this Warrant may be amended, modified or waived only with the written consent of the Holder.

17. REPRESENTATIONS AND COVENANTS OF THE HOLDER. This Preferred Stock Purchase Warrant has been entered into by the Company in reliance upon the following representations and covenants of the Holder, which by its execution hereof the Holder hereby confirms:

A. INVESTMENT PURPOSE. The right to acquire Preferred Stock or the Preferred Stock issuable upon exercise of the Holder's rights contained herein will be acquired for investment and not with a view to the sale or distribution of any part thereof, and the Holder has no present intention of selling or engaging in any public distribution of the same except pursuant to a registration or exemption.

B. ACCREDITED INVESTOR. Holder is an "accredited investor" within the meaning of the Securities and Exchange Rule 501 of Regulation D, as presently in effect.

C. PRIVATE ISSUE. The Holder understands (i) that the Preferred

Stock issuable upon exercise of the Holder's rights contained herein is not registered under the 1933 Act or qualified under applicable state securities laws on the ground that the issuance contemplated by this Warrant will be exempt from the registration and qualifications requirements thereof, and (ii) that the Company's reliance on such exemption is predicated on the representations set forth in this SECTION 17.

D. FINANCIAL RISK. The Holder has such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of its investment and has the ability to bear the economic risks of its investment.

18. NOTICES, TRANSFERS, ETC.

A. Any notice or written communication required or permitted to be given to the Holder may be given by certified mail or delivered to the Holder at the address most recently provided by the Holder to the Company.

B. Subject to compliance with applicable federal and state securities laws, this Warrant may be transferred by the Holder with respect to any or all of the shares purchasable hereunder. Upon surrender of this Warrant to the Company, together with the assignment notice annexed hereto duly executed, for transfer of this Warrant as an entirety by the Holder, the Company shall issue a new warrant of the same denomination to the assignee. Upon surrender of this Warrant to the Company, together with the assignment hereof properly endorsed, by the Holder for transfer with respect to a portion of the shares of Preferred Stock purchasable hereunder, the Company shall issue a new warrant to the assignee, in such denomination as shall be requested by the Holder hereof, and shall issue to such Holder a new warrant covering the number of shares in respect of which this Warrant shall not have been transferred.

C. In case this Warrant shall be mutilated, lost, stolen or destroyed, the Company shall issue a new warrant of like tenor and denomination and deliver the same (i) in exchange and substitution for and upon surrender and cancellation of any mutilated Warrant, or (ii) in lieu of any Warrant lost, stolen or destroyed, upon receipt

of an affidavit of the Holder or other evidence reasonably satisfactory to the Company of the loss, theft or destruction of such Warrant and an indemnification of loss by the Holder in favor of the Company.

19. NO IMPAIRMENT. The Company will not, by amendment of its Articles or through any reclassification, capital reorganization, consolidation, merger, sale or conveyance of assets, dissolution, liquidation, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance of performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such action as may be necessary or appropriate in order to protect the rights of the Holder.

20. GOVERNING LAW. The provisions and terms of this Warrant shall be governed by and construed in accordance with the internal laws of the State of California.

21. SUCCESSORS AND ASSIGNS. This Warrant shall be binding upon the Company's successors and assigns and shall inure to the benefit of the Holder's successors, legal representatives and permitted assigns.

22. BUSINESS DAYS. If the last or appointed day for the taking of any action required or the expiration of any rights granted herein shall be a Saturday or Sunday or a legal holiday in California, then such action may be taken or right may be exercised on the next succeeding day which is not a Saturday or Sunday or such a legal holiday.

23. QUALIFYING PUBLIC OFFERING. If the Company shall effect a firm commitment underwritten public offering of shares of Common Stock which results in the conversion of the Preferred Stock into Common Stock pursuant to the Company's Articles in effect immediately prior to such offering, then, effective upon such conversion, this Warrant shall change from the right to purchase shares of Preferred Stock to the right to purchase shares of Common Stock, and the Holder shall thereupon have the right to purchase; at a total price equal to that payable upon the exercise of this Warrant in full, the number of shares of Common Stock which would have been receivable by the Holder upon the exercise of this Warrant for shares of Preferred Stock immediately prior to such conversion of such shares of Preferred Stock into shares of Common Stock, and in such event appropriate provisions shall be made with respect to the rights and interest of the Holder to the end that the provisions hereof (including, without limitation, the provisions for the adjustment of the Purchase Price and of the number of shares purchasable upon exercise of this Warrant and the provisions

relating to the net issue election) shall thereafter be applicable to any shares of Common Stock deliverable upon the exercise hereof.

24. VALUE. The Company and the Holder agree that the value of this Warrant on the date of grant is $100.

Dated: May , 1997

RIGEL PHARMACEUTICALS, INC.

By: /s/ NJ Montgomery

Name: Nancy Montgomery

Title: Chief Financial Officer

Attest:

/s/ Brian C. Cunningham

Secretary

SUBSCRIPTION

To: Date:

The undersigned hereby subscribes for _____ shares of Preferred Stock covered by this Warrant. The certificate(s) for such shares shall be issued in the name of the undersigned or as otherwise indicated below:

Signature

Name for Registration

Mailing Address

NET ISSUE ELECTION NOTICE

To: Date:

The undersigned hereby elects under SECTION 4 to surrender the right to purchase _____ shares of Preferred Stock pursuant to this Warrant. The certificate(s) for such shares issuable upon such net issue election shall be issued in the name of the undersigned or as otherwise indicated below:

Signature

Name for Registration

Mailing Address

ASSIGNMENT

For value received _____ hereby sells, assigns and transfers unto _____

[Please print or typewrite name and address of Assignee]

the within Warrant, and does hereby irrevocably constitute and appoint

_____ its attorney to transfer the within Warrant on the books of the within named Company with full power of substitution on the premises.

Dated:

In the Presence of:

- ---

EXHIBIT A

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

SEE ATTACHED PAGES.

EXHIBIT B

CAPITALIZATION TABLE

THIS WARRANT HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "1933 ACT"), OR ANY APPLICABLE STATE SECURITIES LAWS, AND MAY NOT BE SOLD OR TRANSFERRED UNLESS SUCH SALE OR TRANSFER IS IN ACCORDANCE WITH THE REGISTRATION REQUIREMENTS OF SUCH ACT AND APPLICABLE LAWS OR SOME OTHER EXEMPTION FROM THE REGISTRATION REQUIREMENTS OF SUCH ACT AND APPLICABLE LAWS IS AVAILABLE WITH RESPECT THERETO.

PREFERRED STOCK PURCHASE WARRANT

Warrant No. _____ Number of Shares: 131,578
Series C Preferred Stock

RIGEL PHARMACEUTICALS, INC.

Void after June 30, 2005

1. ISSUANCE. This Warrant is issued to LIGHTHOUSE CAPITAL PARTNERS II, L.P. by RIGEL PHARMACEUTICALS, INC., a Delaware corporation (hereinafter with its successors called the "COMPANY").

2. PURCHASE PRICE; NUMBER OF SHARES. The registered holder of this Warrant (the "HOLDER"), commencing on the date hereof, is entitled upon surrender of this Warrant with the subscription form annexed hereto duly executed, at the principal office of the Company, to purchase from the Company the following securities (collectively, the "SHARES") at a price per share of $1.14 (the "PURCHASE PRICE"), 131,578 fully paid and nonassessable shares of Series C Preferred Stock, $.001 par value, of the Company (the "PREFERRED STOCK"). Until such time as this Warrant is exercised in full or expires, the Purchase Price and the securities issuable upon exercise of this Warrant are subject to adjustment as hereinafter provided. The person or persons on whose name or names any certificate representing shares of Preferred Stock is issued hereunder shall be deemed to have become the holder of record of the shares represented thereby as at the close of business on the date this Warrant is exercised with respect to such shares, whether or not the transfer books of the Company shall be closed.

3. PAYMENT OF THE PURCHASE PRICE. The Purchase Price may be paid (i) in cash or by check, (ii) by the surrender by the Holder to the Company of any promissory notes or other obligations issued by the Company, with all such notes and obligations so surrendered being credited against the Purchase Price in an amount equal to the principal amount thereof plus accrued interest to the date of surrender, or (iii) by any combination of the foregoing.

4. NET ISSUE ELECTION. The Holder may elect to receive, without the payment by the Holder of any additional consideration, shares of Preferred Stock equal to the value of this Warrant or any portion hereof by the surrender of this Warrant or such portion to the Company, with the net issue election notice annexed hereto duly executed, at the principal office of the Company. Thereupon, the Company shall issue to the Holder such number of fully paid and nonassessable shares of Preferred Stock as is computer using the following formula:

$$X = \frac{Y\ (A - B)}{A}$$

where: X= the number of shares of Preferred Stock to be issued to the Holder pursuant to this SECTION 4.

Y= the number of shares of Preferred Stock covered by this Warrant in respect of which the net issue election is made pursuant to this SECTION 4.

A= the Fair Market Value (defined below) of one share of Preferred Stock, as determined at the time the net issue election is made pursuant to this SECTION 4.

B= the Purchase Price in effect under this Warrant at the time the net issue election is made pursuant to this SECTION 4.

"Fair Market Value" of a share of Preferred Stock (or Common Stock if the Preferred Stock has been automatically converted into Common Stock) as a particular date (the "Determination Date") shall mean:

(i) If the net issue election is made in connection with and

contingent upon the closing of the sale of the Company's Common Stock to the public in a public offering pursuant to a Registration Statement under the Act (a "Public Offering"), and if the Company's Registration Statement relating to such Public Offering ("Registration Statement") has been declared effective by the SEC, the initial "Price to Public" specified in the final prospectus with respect to such offering multiplied by the number of shares of Common Stock into which each share of Preferred Stock is then convertible.

(ii) If the net issue election is not made in connection with and contingent upon a Public Offering, then as follows:

(A) If traded on a securities exchange or the Nasdaq National Market, the fair market value of the Common Stock shall be deemed to be the average of the closing or last reported sale prices of the Common Stock on such exchange or market over the 30-day period ending five business days prior to the Determination Date, and the fair market value of the Preferred Stock shall be deemed to be such fair market value of the Common Stock multiplied by the number of shares of Common Stock into which each share of Preferred Stock is then convertible;

(B) If otherwise traded in an over-the-counter market, the fair market value of the Common Stock shall be deemed to be the average of the closing ask prices of the Common Stock over the 30-day period ending five business days prior to the Determination Date, and the fair market value of the Preferred Stock shall be deemed to be such fair market value of the Common Stock multiplied by the number of shares of Common Stock into which each share of Preferred Stock is then convertible; and

(C) If there is no public market for the Common Stock, then fair market value shall be determined in good faith by the Company's Board of Directors.

5. PARTIAL EXERCISE. This Warrant may be exercised in part, and the Holder shall be entitled to receive a new warrant, which shall be dated as of the date of this Warrant, covering the number of shares in respect of which this Warrant shall not have been exercised.

6. FRACTIONAL SHARES. In no event shall any fractional share of Preferred Stock be issued upon any exercise of this Warrant. If, upon exercise of this Warrant as an entirety, the Holder would, except as provided in this Section 6, be entitled to receive a fractional share of Preferred Stock, then the Company shall pay in lieu thereof, the Fair Market Value of such fractional share in cash.

7. EXPIRATION DATE; AUTOMATIC EXERCISE. Except as otherwise set forth in SECTION 11, this Warrant shall expire at the close of business on June 30, 2005 and shall be void thereafter. Notwithstanding the foregoing, this Warrant shall automatically be deemed to be exercised in full pursuant to the provisions of SECTION 4 hereof, without any

further action on behalf of the Holder, immediately prior to the time this Warrant would otherwise expire pursuant to the preceding sentence or pursuant to SECTION 11.

8. RESERVED SHARES; VALID ISSUANCE. The Company covenants that it will at all times from and after the date hereof reserve and keep available such number of its authorized shares of Preferred Stock and Common Stock, $.001 par value, of the Company (the "COMMON STOCK"), free from all preemptive or similar rights therein, as will be sufficient to permit, respectively, the exercise of this Warrant in full and the conversion into shares of Common Stock of all shares of Preferred Stock receivable upon such exercise. The Company further covenants that such shares as may be issued pursuant to such exercise and/or conversion will, upon issuance, be duly and validly issued, fully paid and nonassessable and free from all takes, liens and charges with respect to the issuance thereof.

9. STOCK SPLITS AND DIVIDENDS. If after the date hereof the Company shall subdivide the Preferred Stock, by split-up or otherwise, or combine the Preferred Stock, or issue additional shares of Preferred Stock in payment of a stock dividend on the Preferred Stock, the number of shares of Preferred Stock issuable in the exercise of this Warrant shall forthwith be proportionately increased in the case of a subdivision or stock dividend, or proportionately increased in the case of a combination, and the Purchase Price shall forthwith be proportionately decreased in the case of a subdivision or stock dividend, or proportionately increased in the case of a combination.

10. ADJUSTMENTS FOR DILUTING ISSUANCES. The other antidilution rights applicable to the Preferred Stock and the Common Stock of the Company are set

forth in the Amended and Restated Certificate of Incorporation, as amended from time to time (the "Articles"), a true and complete copy in its current form which is attached hereto as EXHIBIT A. Such rights shall not be restated, amended or modified in any manner which effects the Holder differently than the holders of Series C Preferred without such Holder's prior written consent. The Company shall promptly provide the Holder hereof with any restatement, amendment or modification to the Articles promptly after the same has been made.

11. MERGERS AND RECLASSIFICATION. If after the date hereof the Company shall enter into any Reorganization (as hereinafter defined), then, as a condition of such Reorganization, lawful provisions shall be made, and duly executed documents evidencing the same from the Company or its successor shall be delivered to the Holder, so that the Holder shall thereafter have the right to purchase, at a total price not to exceed that payable upon the exercise of this Warrant in full, the kind and amount of shares of stock and other securities and property receivable upon such Reorganization by a holder of the number of shares of Preferred Stock which might have been purchased by the Holder immediately prior to such Reorganization, and in any such case appropriate provisions shall be made with respect to the rights and interest of the Holder to the end that the provisions hereof (including without limitation, provisions for the adjustment of the Purchase Price and the number of shares issuable hereunder and the provisions relating to the net issue election) shall thereafter be applicable in relation to any shares of stock or other securities and property thereafter deliverable upon exercise hereof. For the purposes of this SECTION 11, the term "REORGANIZATION" shall include without limitation any reclassification, capital reorganization or change of the Preferred Stock (other than as a result of a subdivision, combination or stock dividend provided for in SECTION 9 hereof), or any consolidation of the Company with, or merger of the Company into, another corporation or other business organization (other than a merger in which the Company is the surviving corporation and which does not result in any reclassification or change of the outstanding Preferred Stock), or any sale or conveyance to another corporation or other business organization of all or substantially all of the assets of the Company.

Notwithstanding the term of this Warrant fixed pursuant to SECTION 7 above and the provisions of this SECTION 11, the right to purchase Preferred Stock as granted herein shall expire, to the extent not previously exercised, immediately upon the closing of a merger or consolidation of the Company with or into another corporation when the Company is not the surviving corporation (other than a merger or consolidation for the principal purpose of changing the domicile of the Company), or the sale of all or substantially all of the Company's capital stock, properties and assets to any other person, in each case where the stockholders of the Company immediately prior to such merger, consolidation or sale of assets own (directly or indirectly) less than 50% of the voting securities of the surviving entity or purchaser of assets in such transaction (collectively, a "Merger"), except to the extent assumed by the successor corporation (or parent thereof) in connection with such Merger. In the event that any outstanding warrants to purchase equity securities of the Company are assumed, this Warrant shall also be similarly assumed.

The Company shall notify the Holder within twenty (20) days of any proposed Merger, and if the Company fails to deliver such notice, then notwithstanding anything to the contrary in this Warrant, the rights to purchase the Company's Preferred Stock (or the share of stock and other securities and property receivable upon such Merger by a holder of the Preferred Stock (the "OTHER CONSIDERATION")) shall not expire. The Holder may exercise the Warrant contingent upon the closing of the Merger. If the Merger does not close within 60 days after notice, any contingent exercise shall be void.

12. CERTIFICATE OF ADJUSTMENT. Whenever the Purchase Price is adjusted, as herein provided, the Company shall promptly deliver to the Holder a certificate of the Company's chief financial officer setting forth the Purchase Price after such adjustment and setting forth a brief statement of the facts requiring such adjustment.

13. NOTICES OF RECORD DATE, ETC. In the event of:

(a) any taking by the Company of a record of the holders of any class of securities for the purpose of determining the holders thereof who are entitled to receive any dividend or other distribution, or any right to subscribe for, purchase, sell or otherwise acquire or dispose of any shares of stock of any class or any other securities or property, or to receive any other right;

(b) any reclassification of the capital stock of the Company, capital reorganization of the Company, consolidation or merger involving the Company, or sale or conveyance of all or substantially all of its assets; or

(c) any voluntary or involuntary dissolution, liquidation or winding-up of the Company;

then in such event the Company will provide or cause to be provided to the Holder a written notice thereof. Such notice shall be provided at least twenty (20) business days prior to the date specified in such notice on which any such action is to be taken.

14. REPRESENTATIONS, WARRANTIES AND COVENANTS. This warrant is issued and delivered by the Company and accepted by each Holder on the basis of the following representations, warranties and covenants made by the Company:

A. The Company has all necessary authority to issue, execute and deliver this Warrant and to perform its obligations hereunder. This Warrant has been duly authorized, issued, executed and delivered by the Company and is the valid and binding obligation of the Company, enforceable in accordance with its terms, except as enforceability may be limited by bankruptcy, insolvency, reorganization or other similar laws of general application affecting the enforcement of Holders rights or by general equity principals or public policy concerns.

B. The shares of Preferred Stock issuable upon the exercise of this Warrant have been duly authorized and reserved for issuance by the Company and, when issued in accordance with the terms hereof, will be validly issued, fully paid and nonassessable.

C. The issuance, execution and delivery of this Warrant do not, and the issuance of the shares of Preferred Stock upon the exercise of this Warrant in accordance with the terms hereof will not, (i) violate or contravene the Company's Articles or by-laws, or any law, statute, regulations, rule, judgment or order applicable to the Company, (ii) violate, contravene or result in a breach or default under any material contract, agreement or instrument to which the Company is a party or by which the Company or any of its assets are bound or (iii) require the consent or approval of or the filing of any notice or registration with any person or entity.

D. So long as this Warrant has not terminated, Holder shall be entitled to receive such financial and other information as the Holder would be entitled to receive under the Series C Preferred Stock Purchase Agreement if Holder were a holder of that number of shares issuable upon full exercise of this Warrant.

E. As of the date hereof, the authorized capital stock of the Company consists of (i) 20,000,000 shares of Common Stock, of which 2,510,000 are issued and outstanding shares, 175,000 shares are reserved for

issuance upon the exercise of that certain Warrant dated May 23, 1997, and 131,578 shares are reserved for issuance upon the exercise of this Warrant and the conversion of the Preferred Stock, (ii) 665,000 shares of Series A Preferred Stock, of which 665,000 are issued and outstanding shares, and (iii) 7,675,000 shares of Series B Preferred Stock, of which 7,500,000 are issued and outstanding shares, and 175,000 shares are reserved for issuance upon the exercise of that certain Warrant dated May 23, 1997 and (iv) 8,000,000 shares of Series C Preferred Stock, of which 7,386,843 are issued and outstanding shares, and 131,578 shares are reserved for issuance upon the exercise of this Warrant. Attached hereto as EXHIBIT B is a capitalization table summarizing the capitalization of the Company.

15. REGISTRATION RIGHTS. The Company grants to the Holder registration rights contained in SECTIONS 2.2, 2.3 and 2.4 of the Company's Amended and Restated Investor Rights Agreement dated as of November 3, 1997 (the "INVESTOR RIGHTS AGREEMENT"), so that (i) the shares of Common Stock issuable upon conversion of the shares of Preferred Stock issuable upon exercise of this Warrant shall be "Registrable Securities," and (ii) the Holder shall be a "Holder" and "Investor" for all purposes of such Investor Rights Agreement.

16. AMENDMENT. The terms of this Warrant may be amended, modified or waived only with the written consent of the Holder.

17. REPRESENTATIONS AND COVENANTS OF THE HOLDER. The Preferred Stock Purchase Warrant has been entered into by the Company in reliance upon the following representations and covenants of the Holder, which by its execution hereof the Holder hereby confirms:

A. INVESTMENT PURPOSE. The right to acquire Preferred Stock or the Preferred Stock issuable upon exercise of the Holders' rights contained herein will be acquired for investment and not with a view to the sale or distribution of any part thereof, and the Holder has not present intention of selling or engaging in any public distribution of the same except pursuant to a registration or exemption.

B. ACCREDITED INVESTOR. Holder is an "accredited investor" within the meaning of the Securities and Exchange Rule 501 of Regulation D, as

presently in effect.

C. PRIVATE ISSUE. The Holder understands (i) that the Preferred Stock issuable upon exercise of the Holder's rights contained herein is not registered under the 1933 Act or qualified under applicable state securities laws on the ground that the issuance contemplated by this Warrant will be exempt from the registration and qualifications requirements thereof, and (ii) that the Company's reliance on such exemption is predicated on the representations set forth in this SECTION 17.

D. FINANCIAL RISK. The Holder has such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of its investment and has the ability to bear the economic risks of its investment.

18. NOTICES, TRANSFERS, ETC.

A. Any notice or written communication required or permitted to be given to the Holder may be given by certified mail or delivered to the Holder at the address most recently provided by the Holder to the Company.

B. Subject to compliance with applicable federal and state securities laws, this Warrant may be transferred by the Holder with respect to any or all of the shares purchasable hereunder. Upon surrender of this Warrant to the Company, together with the assignment notice annexed hereto duly executed, for transfer of this Warrant as an entirety by the Holder, the Company shall issue a new warrant of the same denomination to the assignee. Upon surrender of this Warrant to the Company, together with the assignment hereof properly endorsed by the Holder for transfer with respect to a portion of the shares of the Preferred Stock purchasable hereunder, the Company shall issue a new warrant to the assignee, in such denomination as shall be requested by the Holder hereof, and shall issue to such Holder a new warrant covering the number of shares in respect of which this Warrant shall not have been transferred.

C. In case this Warrant shall be mutilated, lost, stolen or destroyed, the Company shall issue a new warrant of like tenor and denomination and deliver the same (i) in exchange and substitution for and upon surrender

and cancellation of any mutilated Warrant, or (ii) in lieu of any Warrant lost, stolen or destroyed, upon receipt of any affidavit of the Holder or other evidence reasonably satisfactory to the Company of the loss, theft or destruction of such Warrant and an indemnification of loss by the Holder in favor of the Company.

19. NO IMPAIRMENT. The Company will not, by amendment of its Articles or through any reclassification, capital reorganization, consolidation, merger, sale or conveyance of assets, dissolution, liquidation, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance of performance of any of the terms of this Warrant, but will at all times in good faith assist in the carrying out of all such terms and in the taking of all such action as may be necessary or appropriate in order to protect the rights of the Holder.

20. GOVERNING LAW. The provisions and terms of this Warrant shall be governed by and construed in accordance with the internal laws of the State of California.

21. SUCCESSORS AND ASSIGNS. This Warrant shall be binding upon the Company's successors and assigns and shall inure to the benefit of the Holder's successors, legal representatives and permitted assigns.

22. BUSINESS DAYS. If the last or appointed day for the taking of any action required or the expiration of any rights granted herein shall be a Saturday or Sunday or a legal holiday in California, then such action may be taken or right may be exercised on the next succeeding day which is not a Saturday or Sunday or such a legal holiday.

23. QUALIFYING PUBLIC OFFERING. If the Company shall effect a firm commitment underwritten public offering of shares of Common Stock which results in the conversion of the Preferred Stock into Common Stock pursuant to the Company's Articles in effect immediately prior to such offering, then, effective upon such conversion, this Warrant shall change from the right to Purchase shares of Preferred Stock to the right to purchase shares of Common Stock, and the Holder shall thereupon have the right to purchase, at a total price equal to that payable upon the exercise of this Warrant in full, the number of shares of Common Stock which would have been receivable by the Holder upon the exercise of this Warrant for shares of Preferred Stock immediately prior to such conversion of such shares of Preferred Stock into shares of Common Stock, and in such event appropriate provisions shall be made with respect to the rights and interest of the Holder to the end that the provisions hereof (including, without limitation, the provisions for the

adjustment of the Purchase Price and of the number of shares purchasable upon exercise of this Warrant and the provisions relating to the net issue election) shall thereafter be applicable to any shares of Common Stock deliverable upon the exercise hereof.

24. VALUE. The Company and the Holder agree that the value of this Warrant on the date of grant is $100.

Dated: July 16, 1998

RIGEL PHARMACEUTICALS, INC.

By: /s/ Nancy Montgomery

Name: Nancy Montgomery

Title: Chief Financial Officer

Attest:

- ---

Exhibit 4.6

NO. PDW-____

THE SECURITIES REPRESENTED BY THIS CERTIFICATE HAVE BEEN ACQUIRED FOR INVESTMENT AND HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933 OR ANY STATE SECURITIES LAWS. SUCH SECURITIES MAY NOT BE SOLD OR TRANSFERRED IN THE ABSENCE OF SUCH REGISTRATION OR AN EXEMPTION THEREFROM UNDER SAID ACT AND ANY APPLICABLE STATE SECURITIES LAWS.

WARRANT TO PURCHASE SHARES
OF SERIES D PREFERRED STOCK OF
RIGEL PHARMACEUTICALS, INC.
(VOID AFTER DECEMBER __, 2003)

This certifies that _____ or its assigns (the "Holder"), for value received, is entitled to purchase from RIGEL PHARMACEUTICALS, INC., a Delaware corporation (the "Company"), up to the Maximum Purchase Amount (as defined below) of fully paid and nonassessable shares of the Company's Series D Preferred Stock ("Preferred Stock") for cash, unless exercised as provided in Section 1.2 of this Warrant, at a price equal to the price at which the Company first sells shares of it Series D Preferred Stock after the date of this Warrant, but not greater than Two Dollars ($2.00) per share prior to any adjustments made pursuant to Section 3 of this Warrant (the "Stock Purchase Price") at any time or from time to time up to and including 5:00 p.m. (Pacific time) on the earlier of (i) the closing of the initial public offering of the Company's Common Stock pursuant to a registration statement under the Securities Act of 1933, as amended (the "Initial Public Offering"), (ii) an Organic Change (as provided in Section 3.3 of this Warrant), or (iii) five (5) years from the date of this Warrant, such earlier day being referred to herein as the "Expiration Date", upon surrender to the Company at its principal office (or at such other location as the Company may advise the Holder in writing) of this Warrant properly endorsed with the Form of Subscription attached hereto duly filled in and signed and, if applicable, upon payment in cash or by check of the aggregate Stock Purchase Price for the number of shares for which this Warrant is being exercised determined in accordance with the provisions hereof. The Company shall deliver notice of the Initial Public Offering or Organic Change to the Holder at least 20 days prior to the closing thereof. The Maximum Purchase Amount shall be determined by multiplying (i) the principal amount loaned to the Company pursuant to that certain Convertible Promissory Note entered into by the Company and the Holder on even date herewith (the "Note") by (ii) 10.0%, and dividing the product of (i) and (ii) by the Stock Purchase Price. The Stock Purchase Price and the number of shares purchasable hereunder are subject to adjustment as provided in Section 3 of this Warrant.

This Warrant is subject to the following terms and conditions:

1. EXERCISE; ISSUANCE OF CERTIFICATES; PAYMENT FOR SHARES.

1.1 GENERAL. This Warrant is exercisable at the option of the holder of record hereof, at any time or from time to time, up to the Expiration Date for all or any part of the shares

of Preferred Stock (but not for a fraction of a share) which may be purchased hereunder. The Company agrees that the shares of Preferred Stock purchased under this Warrant shall be and are deemed to be issued to the Holder hereof as the record owner of such shares as of the close of business on the date on which this Warrant shall have been surrendered, properly endorsed, the completed, executed Form of Subscription delivered and payment made for such shares. Certificates for the shares of Preferred Stock so purchased, together with any other securities or property to which the Holder hereof is entitled upon such exercise, shall be delivered to the Holder hereof by the Company at the Company's expense within a reasonable time after the rights represented by this Warrant have been so exercised. In case of a purchase of less than all the shares which may be purchased under this Warrant, the Company shall cancel this Warrant and execute and deliver a new Warrant or Warrants of like tenor for the balance of the shares purchasable under the Warrant surrendered upon such purchase to the Holder hereof within a reasonable time. Each stock certificate so delivered shall be in such denominations of Preferred Stock as may be requested by the Holder hereof and shall be registered in the name of such Holder.

1.2 NET ISSUE EXERCISE. Notwithstanding any provisions herein to the contrary, if the fair market value of one share of the Company's Preferred Stock is greater than the Stock Purchase Price (at the date of calculation as set forth below), in lieu of exercising this Warrant for cash, the Holder may elect to receive shares equal to the value (as determined below) of this Warrant (or the portion thereof being canceled) by surrender of this Warrant at the

principal office of the Company together with the properly endorsed Form of Subscription and notice of such election, in which event the Company shall issue to the Holder a number of shares of Preferred Stock computed using the following formula:

$$X = \frac{Y\,(A-B)}{A}$$

Where X = the number of shares of Preferred Stock to be issued to the Holder

Y = the number of shares of Preferred Stock purchasable under the Warrant or, if only a portion of the Warrant is being exercised, the portion of the Warrant being canceled (at the date of such calculation)

A = the fair market value of one share of the Company's Preferred Stock (at the date of such calculation)

B = Stock Purchase Price (as adjusted to the date of such calculation)

For purposes of the above calculation, fair market value of one share of Preferred Stock shall be determined by the Company's Board of Directors in good faith; provided, however, that in the event the Company makes an initial public offering of its Common Stock the fair market value per share shall be the product of (i) the per share offering price to the public of the Company's initial

public offering, and (ii) the number of shares of Common Stock into which each share of Preferred Stock is convertible at the time of such exercise.

2. SHARES TO BE FULLY PAID; RESERVATION OF SHARES. The Company covenants and agrees that all shares of Preferred Stock which may be issued upon the exercise of the rights represented by this Warrant will, upon issuance, be duly authorized, validly issued, fully paid and nonassessable and free from all preemptive rights of any shareholder and free of all taxes, liens and charges with respect to the issue thereof. The Company further covenants and agrees that, during the period within which the rights represented by this Warrant may be exercised, the Company will at all times have authorized and reserved, for the purpose of issue or transfer upon exercise of the subscription rights evidenced by this Warrant, a sufficient number of shares of authorized but unissued Preferred Stock, or other securities and property, when and as required to provide for the exercise of the rights represented by this Warrant. The Company will take all such action as may be necessary to assure that such shares of Preferred Stock may be issued as provided herein without violation of any applicable law or regulation, or of any requirements of any domestic securities exchange upon which the Preferred Stock may be listed; provided, however, that the Company shall not be required to effect a registration under Federal or State securities laws with respect to such exercise. The Company will not take any action which would result in any adjustment of the Stock Purchase Price (as set forth in Section 3 hereof) (i) if the total number of shares of Preferred Stock issuable after such action upon exercise of all outstanding warrants, together with all shares of Preferred Stock then outstanding and all shares of Preferred Stock then issuable upon exercise of all options and upon the conversion of all convertible securities then outstanding, would exceed the total number of shares of Preferred Stock then authorized by the Company's Certificate of Incorporation, or (ii) if the total number of shares of Common Stock issuable after such action upon the conversion of all such shares of Preferred Stock, together with all shares of Common Stock then issuable upon exercise of all options and upon the conversion of all such shares of Preferred Stock, together with all shares of Common Stock then outstanding and all shares of Common Stock then issuable upon exercise of all options and upon the conversion of all convertible securities then outstanding would exceed the total number of shares of Common Stock then authorized by the Company's Certificate of Incorporation.

3. ADJUSTMENT OF STOCK PURCHASE PRICE AND NUMBER OF SHARES. The Stock Purchase Price and the number of shares purchasable upon the exercise of this Warrant shall be subject to adjustment from time to time upon the occurrence of certain events described in this Section 3. Upon each adjustment of the Stock Purchase Price, the Holder of this Warrant shall thereafter be entitled to purchase, at the Stock Purchase Price resulting from such adjustment, the number of shares obtained by multiplying the Stock Purchase Price in effect immediately prior to such adjustment by the number of shares purchasable pursuant hereto immediately prior to such adjustment, and dividing the product thereof by the Stock Purchase Price resulting from

such adjustment.

3.1 SUBDIVISION OR COMBINATION OF STOCK. In case the Company shall at any time subdivide its outstanding shares of Preferred Stock into a greater number of shares, the

Stock Purchase Price in effect immediately prior to such subdivision shall be proportionately reduced, and conversely, in case the outstanding shares of Preferred Stock of the Company shall be combined into a smaller number of shares, the Stock Purchase Price in effect immediately prior to such combination shall be proportionately increased.

3.2 DIVIDENDS IN PREFERRED STOCK, OTHER STOCK, PROPERTY, RECLASSIFICATION. If at any time or from time to time the Holders of Preferred Stock (or any shares of stock or other securities at the time receivable upon the exercise of this Warrant) shall have received or become entitled to receive, without payment therefor,

(a) Preferred Stock or any shares of stock or other securities which are at any time directly or indirectly convertible into or exchangeable for Preferred Stock, or any rights or options to subscribe for, purchase or otherwise acquire any of the foregoing by way of dividend or other distribution,

(b) any cash paid or payable otherwise than as a cash dividend, or

(c) Preferred Stock or additional stock or other securities or property (including cash) by way of spinoff, split-up, reclassification, combination of shares or similar corporate rearrangement, (other than shares of Preferred Stock issued as a stock split or adjustments in respect of which shall be covered by the terms of Section 3.1 above), then and in each such case, the Holder hereof shall, upon the exercise of this Warrant, be entitled to receive, in addition to the number of shares of Preferred Stock receivable thereupon, and without payment of any additional consideration therefor, the amount of stock and other securities and property (including cash in the cases referred to in clause (b) above and this clause (c)) which such Holder would hold on the date of such exercise had he been the holder of record of such Preferred Stock as of the date on which holders of Preferred Stock received or became entitled to receive such shares or all other additional stock and other securities and property.

3.3 REORGANIZATION, RECLASSIFICATION, CONSOLIDATION, MERGER OR SALE. If any recapitalization, reclassification or reorganization of the capital stock of the Company, or any consolidation or merger of the Company with another corporation, or the sale of all or substantially all of its assets or other transaction shall be effected in such a way that holders of Preferred Stock shall be entitled to receive stock, securities, or other assets or property (an "Organic Change"), then, as a condition of such Organic Change, lawful and adequate provisions shall be made by the Company whereby the Holder hereof shall thereafter have the right to purchase and receive (in lieu of the shares of the Preferred Stock of the Company immediately theretofore purchasable and receivable upon the exercise of the rights represented hereby) such shares of stock, securities or other assets or property as may be issued or payable with respect to or in exchange for a number of outstanding shares of such Preferred Stock equal to the number of shares of such stock immediately theretofore purchasable and receivable upon the exercise of the rights represented hereby; provided, however, that in the event the value of the stock, securities or other assets or property (determined in good faith by the Board of Directors of the Company) issuable or payable with respect to one share of the Preferred Stock of the Company immediately theretofore purchasable and receivable upon the exercise of the rights represented hereby is in

excess of the Stock Purchase Price hereof effective at the time of a merger, and securities received in such reorganization, if any, are publicly traded, then this Warrant shall expire unless exercised prior to such Organic Change. In the event of any Organic Change, appropriate provision shall be made by the Company with respect to the rights and interests of the Holder of this Warrant to the end that the provisions hereof (including, without limitation, provisions for adjustments of the Stock Purchase Price and of the number of shares purchasable and receivable upon the exercise of this Warrant) shall thereafter be applicable, in relation to any shares of stock, securities or assets thereafter deliverable upon the exercise hereof. The Company will not effect any such consolidation, merger or sale unless, prior to the consummation thereof, the successor corporation (if other than the Company) resulting from such consolidation or the corporation purchasing such assets

shall assume by written instrument reasonably satisfactory in form and substance to the Holders of a majority of the warrants to purchase Preferred Stock then outstanding, executed and mailed or delivered to the registered Holder hereof at the last address of such Holder appearing on the books of the Company, the obligation to deliver to such Holder such shares of stock, securities or assets as, in accordance with the foregoing provisions, such Holder may be entitled to purchase.

3.4 CERTAIN EVENTS. If any change in the outstanding Preferred Stock of the Company or any other event occurs as to which the other provisions of this Section 3 are not strictly applicable or if strictly applicable would not fairly protect the purchase rights of the Holder of the Warrant in accordance with such provisions, then the Board of Directors of the Company shall make an adjustment in the number and class of shares available under the Warrant, the Stock Purchase Price or the application of such provisions, so as to protect such purchase rights as aforesaid. The adjustment shall be such as will give the Holder of the Warrant upon exercise for the same aggregate Stock Purchase Price the total number, class and kind of shares as he would have owned had the Warrant been exercised prior to the event and had he continued to hold such shares until after the event requiring adjustment.

3.5 NOTICES OF CHANGE.

(a) Immediately upon any adjustment in the number or class of shares subject to this Warrant and of the Stock Purchase Price, the Company shall give written notice thereof to the Holder, setting forth in reasonable detail and certifying the calculation of such adjustment.

(b) The Company shall give written notice to the Holder at least 20 business days prior to the date on which the Company closes its books or takes a record for determining rights to receive any dividends or distributions.

(c) The Company shall also give written notice to the Holder at least 20 business days prior to the date on which an Organic Change shall take place.

4. ISSUE TAX. The issuance of certificates for shares of Preferred Stock upon the exercise of the Warrant shall be made without charge to the Holder of the Warrant for any issue tax (other than any applicable income taxes) in respect thereof; provided, however, that the

Company shall not be required to pay any tax which may be payable in respect of any transfer involved in the issuance and delivery of any certificate in a name other than that of the then Holder of the Warrant being exercised.

5. CLOSING OF BOOKS. The Company will at no time close its transfer books against the transfer of any warrant or of any shares of Preferred Stock issued or issuable upon the exercise of any warrant in any manner which interferes with the timely exercise of this Warrant.

6. NO VOTING OR DIVIDEND RIGHTS; LIMITATION OF LIABILITY. Nothing contained in this Warrant shall be construed as conferring upon the Holder hereof the right to vote or to consent or to receive notice as a shareholder of the Company or any other matters or any rights whatsoever as a shareholder of the Company. No dividends or interest shall be payable or accrued in respect of this Warrant or the interest represented hereby or the shares purchasable hereunder until, and only to the extent that, this Warrant shall have been exercised. No provisions hereof, in the absence of affirmative action by the Holder to purchase shares of Preferred Stock, and no mere enumeration herein of the rights or privileges of the Holder hereof, shall give rise to any liability of such Holder for the Stock Purchase Price or as a shareholder of the Company, whether such liability is asserted by the Company or by its creditors.

7. WARRANTS TRANSFERABLE. Subject to compliance with applicable federal and state securities laws, this Warrant and all rights hereunder are transferable, in whole or in part, without charge to the holder hereof (except for transfer taxes), upon surrender of this Warrant properly endorsed. Each taker and holder of this Warrant, by taking or holding the same, consents and agrees that this Warrant, when endorsed in blank, shall be deemed negotiable, and that the holder hereof, when this Warrant shall have been so endorsed, may be treated by the Company, at the Company's option, and all other persons dealing with this Warrant as the absolute owner hereof for any purpose and as the person entitled to exercise the rights represented by this Warrant, or to the transfer hereof on the books of the Company any notice to the contrary notwithstanding; but until such transfer on such books, the Company may treat the registered owner hereof as the owner for all purposes.

8. RIGHTS AND OBLIGATIONS SURVIVE EXERCISE OF WARRANT. The rights and obligations of the Company, of the holder of this Warrant and of the holder of shares of Preferred Stock issued upon exercise of this Warrant, shall survive the exercise of this Warrant.

9. MODIFICATION AND WAIVER. This Warrant and any provision hereof may be changed, waived, discharged or terminated only by an instrument in writing signed by the party against which enforcement of the same is sought.

10. NOTICES. Any notice, request or other document required or permitted to be given or delivered to the holder hereof or the Company shall be delivered or shall be sent by certified mail, postage prepaid, to each such holder at its address as shown on the books of the Company or to the Company at the address indicated therefor in the first paragraph of this Warrant or such other address as either may from time to time provide to the other.

11. BINDING EFFECT ON SUCCESSORS. This Warrant shall be binding upon any corporation succeeding the Company by merger, consolidation or acquisition of all or substantially all of the Company's assets. All of the obligations of the Company relating to the Preferred Stock issuable upon the exercise of this Warrant shall survive the exercise and termination of this Warrant. All of the covenants and agreements of the Company shall inure to the benefit of the successors and assigns of the holder hereof.

12. DESCRIPTIVE HEADINGS AND GOVERNING LAW. The description headings of the several sections and paragraphs of this Warrant are inserted for convenience only and do not constitute a part of this Warrant. This Warrant shall be construed and enforced in accordance with, and the rights of the parties shall be governed by, the laws of the State of California.

13. LOST WARRANTS. The Company represents and warrants to the Holder hereof that upon receipt of evidence reasonably satisfactory to the Company of the loss, theft, destruction, or mutilation of this Warrant and, in the case of any such loss, theft or destruction, upon receipt of an indemnity reasonably satisfactory to the Company, or in the case of any such mutilation upon surrender and cancellation of such Warrant, the Company, at its expense, will make and deliver a new Warrant, of like tenor, in lieu of the lost, stolen, destroyed or mutilated Warrant.

14. FRACTIONAL SHARES. No fractional shares shall be issued upon exercise of this Warrant. The Company shall, in lieu of issuing any fractional share, pay the holder entitled to such fraction a sum in cash equal to such fraction multiplied by the then effective Stock Purchase Price.

15. MARKET STANDOFF. The Holder of this Warrant, by acceptance hereof, agrees that such Holder will not, without the prior written consent of the lead underwriter of the Company's initial public offering, directly or indirectly offer to sell, contract to sell (including, without limitation, any short sale), grant any option for the sale of, acquire any option to dispose of, or otherwise dispose of any shares subject to this Warrant for a period of 180 days following the day on which the registration statement filed on behalf of the Company in connection with the initial public offering shall become effective by order of the Securities and Exchange Commission.

[THIS SPACE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, the Company has caused this Warrant to be duly executed by its officers, thereunto duly authorized this 4th day of December, 1998.

RIGEL PHARMACEUTICALS, INC.
A Delaware corporation

By: _____

Title: _____

ATTEST:

_____
Secretary

EXHIBIT A

SUBSCRIPTION FORM

Date: _____, 19___

Rigel Pharmaceuticals, Inc.
772 Lucerne Drive
Sunnyvale, CA 94086

Attn: President

Ladies and Gentlemen:

/ / The undersigned hereby elects to exercise the warrant issued to it by Rigel Pharmaceuticals, Inc. (the "Company") and dated _____ _____, ____ Warrant No. PDW-___ (the "Warrant") and to purchase thereunder _____ shares of the Series D Preferred Stock of the Company (the "Shares") at a purchase price of _____ Dollars ($_____) per Share or an aggregate purchase price of _____ Dollars ($_____) (the "Purchase Price").

/ / The undersigned hereby elects to convert _____ percent (____%) of the value of the Warrant pursuant to the provisions of Section 1.2 of the Warrant.

Pursuant to the terms of the Warrant, and unless exercised pursuant to Section 1.2 of the Warrant, the undersigned has delivered the Purchase Price herewith in full in cash or by certified check or wire transfer.

Very truly yours,

_____

By: _____

Title:_____

EXHIBIT 10.1

INDEMNITY AGREEMENT

THIS AGREEMENT is made and entered into this ____ day of _____, 2000 by and between RIGEL PHARMACEUTICALS, INC. a Delaware corporation (the "Corporation"), and _____ ("Agent").

RECITALS

WHEREAS, Agent performs a valuable service to the Corporation in his/her capacity as _____ of the Corporation;

WHEREAS, the stockholders of the Corporation have adopted bylaws (the "Bylaws") providing for the indemnification of the directors, officers, employees and other agents of the Corporation, including persons serving at the request of the Corporation in such capacities with other corporations or enterprises, as authorized by the Delaware General Corporation Law, as amended (the "Code");

WHEREAS, the Bylaws and the Code, by their non-exclusive nature, permit contracts between the Corporation and its agents, officers, employees and other agents with respect to indemnification of such persons; and

WHEREAS, in order to induce Agent to continue to serve as _____ of the Corporation, the Corporation has determined and agreed to enter into this Agreement with Agent;

NOW, THEREFORE, in consideration of Agent's continued service as _____ after the date hereof, the parties hereto agree as follows:

AGREEMENT

1. SERVICES TO THE CORPORATION. Agent will serve, at the will of the Corporation or under separate contract, if any such contract exists, as _____ of the Corporation or as a director, officer or other fiduciary of an affiliate of the Corporation (including any employee benefit plan of the Corporation) faithfully and to the best of his ability so long as he is duly elected and qualified in accordance with the provisions of the Bylaws or other applicable charter documents of the Corporation or such affiliate; PROVIDED, HOWEVER, that Agent may at any time and for any reason resign from such position (subject to any contractual obligation that Agent may have assumed apart from this Agreement) and that the Corporation or any affiliate shall have no obligation under this Agreement to continue Agent in any such position.

2. INDEMNITY OF AGENT. The Corporation hereby agrees to hold harmless and indemnify Agent to the fullest extent authorized or permitted by the provisions of the Bylaws and the Code, as the same may be amended from time to time (but, only to the extent that such amendment permits the Corporation to provide broader indemnification rights than the Bylaws or the Code permitted prior to adoption of such amendment).

3. ADDITIONAL INDEMNITY. In addition to and not in limitation of the indemnification otherwise provided for herein, and subject only to the exclusions set forth in Section 4 hereof, the Corporation hereby further agrees to hold harmless and indemnify Agent:

(a) against any and all expenses (including attorneys' fees), witness fees, damages, judgments, fines and amounts paid in settlement and any other amounts that Agent becomes legally obligated to pay because of any claim or claims made against or by him in connection with any threatened, pending or completed action, suit or proceeding, whether civil, criminal, arbitrational, administrative or investigative (including an action by or in the right of the Corporation) to which Agent is, was or at any time becomes a party, or is threatened to be made a party, by reason of the fact that Agent is, was or at any time becomes a director, officer, employee or other agent of Corporation, or is or was serving or at any time serves at the request of the Corporation as a director, officer, employee or other agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise; and

(b) otherwise to the fullest extent as may be provided to Agent by the Corporation under the non-exclusivity provisions of the Code and Section 43 of the Bylaws.

4. LIMITATIONS ON ADDITIONAL INDEMNITY. No indemnity pursuant to Section 3 hereof shall be paid by the Corporation:

(a) on account of any claim against Agent for an accounting of profits made from the purchase or sale by Agent of securities of the Corporation pursuant to the provisions of Section 16(b) of the Securities Exchange Act of

1934 and amendments thereto or similar provisions of any federal, state or local statutory law;

(b) on account of Agent's conduct that was knowingly fraudulent or deliberately dishonest or that constituted willful misconduct;

(c) on account of Agent's conduct that constituted a breach of Agent's duty of loyalty to the Corporation or resulted in any personal profit or advantage to which Agent was not legally entitled;

(d) for which payment is actually made to Agent under a valid and collectible insurance policy or under a valid and enforceable indemnity clause, bylaw or agreement, except in respect of any excess beyond payment under such insurance, clause, bylaw or agreement;

(e) if indemnification is not lawful (and, in this respect, both the Corporation and Agent have been advised that the Securities and Exchange Commission believes that indemnification for liabilities arising under the federal securities laws is against public policy and is, therefore, unenforceable and that claims for indemnification should be submitted to appropriate courts for adjudication); or

(f) in connection with any proceeding (or part thereof) initiated by Agent, or any proceeding by Agent against the Corporation or its directors, officers, employees or other agents, unless (i) such indemnification is expressly required to be made by law, (ii) the proceeding was authorized by the Board of Directors of the Corporation, (iii) such indemnification is provided by the Corporation, in its sole discretion, pursuant to the powers

vested in the Corporation under the Code, or (iv) the proceeding is initiated pursuant to Section 9 hereof.

5. CONTINUATION OF INDEMNITY. All agreements and obligations of the Corporation contained herein shall continue during the period Agent is a director, officer, employee or other agent of the Corporation (or is or was serving at the request of the Corporation as a director, officer, employee or other agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise) and shall continue thereafter so long as Agent shall be subject to any possible claim or threatened, pending or completed action, suit or proceeding, whether civil, criminal, arbitrational, administrative or investigative, by reason of the fact that Agent was serving in the capacity referred to herein.

6. PARTIAL INDEMNIFICATION. Agent shall be entitled under this Agreement to indemnification by the Corporation for a portion of the expenses (including attorneys' fees), witness fees, damages, judgments, fines and amounts paid in settlement and any other amounts that Agent becomes legally obligated to pay in connection with any action, suit or proceeding referred to in Section 3 hereof even if not entitled hereunder to indemnification for the total amount thereof, and the Corporation shall indemnify Agent for the portion thereof to which Agent is entitled.

7. NOTIFICATION AND DEFENSE OF CLAIM. Not later than thirty (30) days after receipt by Agent of notice of the commencement of any action, suit or proceeding, Agent will, if a claim in respect thereof is to be made against the Corporation under this Agreement, notify the Corporation of the commencement thereof; but the omission so to notify the Corporation will not relieve it from any liability which it may have to Agent otherwise than under this Agreement. With respect to any such action, suit or proceeding as to which Agent notifies the Corporation of the commencement thereof:

(a) the Corporation will be entitled to participate therein at its own expense;

(b) except as otherwise provided below, the Corporation may, at its option and jointly with any other indemnifying party similarly notified and electing to assume such defense, assume the defense thereof, with counsel reasonably satisfactory to Agent. After notice from the Corporation to Agent of its election to assume the defense thereof, the Corporation will not be liable to Agent under this Agreement for any legal or other expenses subsequently incurred by Agent in connection with the defense thereof except for reasonable costs of investigation or otherwise as provided below. Agent shall have the right to employ separate counsel in such action, suit or proceeding but the fees and expenses of such counsel incurred after notice from the Corporation of its assumption of the defense thereof shall be at the expense of Agent unless (i) the employment of counsel by Agent has been authorized by the Corporation, (ii) Agent shall have reasonably concluded that there may be a conflict of interest between the Corporation and Agent in the conduct of the defense of such action or (iii) the Corporation shall not in fact have employed counsel to assume the defense of such action, in each of which cases the fees and expenses of Agent's separate counsel shall be at the expense of the Corporation. The Corporation shall not be entitled to assume the defense of any action, suit or proceeding

brought by or on behalf of the Corporation or as to which Agent shall have made the conclusion provided for in clause (ii) above; and

(c) the Corporation shall not be liable to indemnify Agent under this Agreement for any amounts paid in settlement of any action or claim effected without its written consent, which shall not be unreasonably withheld. The Corporation shall be permitted to settle any action except that it shall not settle any action or claim in any manner which would impose any penalty or limitation on Agent without Agent's written consent, which may be given or withheld in Agent's sole discretion.

8. EXPENSES. The Corporation shall advance, prior to the final disposition of any proceeding, promptly following request therefor, all expenses incurred by Agent in connection with such proceeding upon receipt of an undertaking by or on behalf of Agent to repay said amounts if it shall be determined ultimately that Agent is not entitled to be indemnified under the provisions of this Agreement, the Bylaws, the Code or otherwise.

9. ENFORCEMENT. Any right to indemnification or advances granted by this Agreement to Agent shall be enforceable by or on behalf of Agent in any court of competent jurisdiction if (i) the claim for indemnification or advances is denied, in whole or in part, or (ii) no disposition of such claim is made within ninety (90) days of request therefor. Agent, in such enforcement action, if successful in whole or in part, shall be entitled to be paid also the expense of prosecuting his claim. It shall be a defense to any action for which a claim for indemnification is made under Section 3 hereof (other than an action brought to enforce a claim for expenses pursuant to Section 8 hereof, provided that the required undertaking has been tendered to the Corporation) that Agent is not entitled to indemnification because of the limitations set forth in Section 4 hereof. Neither the failure of the Corporation (including its Board of Directors or its stockholders) to have made a determination prior to the commencement of such enforcement action that indemnification of Agent is proper in the circumstances, nor an actual determination by the Corporation (including its Board of Directors or its stockholders) that such indemnification is improper shall be a defense to the action or create a presumption that Agent is not entitled to indemnification under this Agreement or otherwise.

10. SUBROGATION. In the event of payment under this Agreement, the Corporation shall be subrogated to the extent of such payment to all of the rights of recovery of Agent, who shall execute all documents required and shall do all acts that may be necessary to secure such rights and to enable the Corporation effectively to bring suit to enforce such rights.

11. NON-EXCLUSIVITY OF RIGHTS. The rights conferred on Agent by this Agreement shall not be exclusive of any other right which Agent may have or hereafter acquire under any statute, provision of the Corporation's Certificate of Incorporation or Bylaws, agreement, vote of stockholders or directors, or otherwise, both as to action in his official capacity and as to action in another capacity while holding office.

12. SURVIVAL OF RIGHTS.

(a) The rights conferred on Agent by this Agreement shall continue after Agent has ceased to be a director, officer, employee or other agent of the Corporation or to serve at the request of the Corporation as a director, officer, employee or other agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise and shall inure to the benefit of Agent's heirs, executors and administrators.

(b) The Corporation shall require any successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business or assets of the Corporation, expressly to assume and agree to perform this Agreement in the same manner and to the same extent that the Corporation would be required to perform if no such succession had taken place.

13. SEPARABILITY. Each of the provisions of this Agreement is a separate and distinct agreement and independent of the others, so that if any provision hereof shall be held to be invalid for any reason, such invalidity or unenforceability shall not affect the validity or enforceability of the other provisions hereof. Furthermore, if this Agreement shall be invalidated in its entirety on any ground, then the Corporation shall nevertheless indemnify Agent to the fullest extent provided by the Bylaws, the Code or any other applicable law.

14. GOVERNING LAW. This Agreement shall be interpreted and enforced in accordance with the laws of the State of Delaware.

15. AMENDMENT AND TERMINATION. No amendment, modification, termination

or cancellation of this Agreement shall be effective unless in writing signed by both parties hereto.

16. IDENTICAL COUNTERPARTS. This Agreement may be executed in one or more counterparts, each of which shall for all purposes be deemed to be an original but all of which together shall constitute but one and the same Agreement. Only one such counterpart need be produced to evidence the existence of this Agreement.

17. HEADINGS. The headings of the sections of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction hereof.

18. NOTICES. All notices, requests, demands and other communications hereunder shall be in writing and shall be deemed to have been duly given (i) upon delivery if delivered by hand to the party to whom such communication was directed or (ii) upon the third business day after the date on which such communication was mailed if mailed by certified or registered mail with postage prepaid:

(a) If to Agent, at the address indicated on the signature page hereof.

(b) If to the Corporation, to

Rigel Pharmaceuticals, Inc.
240 East Grand Avenue
South San Francisco, CA 94080

or to such other address as may have been furnished to Agent by the Corporation.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement on and as of the day and year first above written.

RIGEL PHARMACEUTICALS, INC.

By: _____

Title: _____

AGENT

_____

Address:

_____

_____

EXHIBIT 10.2

RIGEL PHARMACEUTICALS, INC.

2000 EQUITY INCENTIVE PLAN

ADOPTED JANUARY 27, 2000
APPROVED BY STOCKHOLDERS MARCH 15, 2000
TERMINATION DATE: JANUARY 26, 2010

1. PURPOSES.

(a) The Plan is an amendment and restatement of, and is intended to supersede and replace, the Company's 1997 Stock Option Plan.

(b) The persons eligible to receive Stock Awards are the Employees, Directors and Consultants of the Company and its Affiliates.

(c) The purpose of the Plan is to provide a means by which eligible recipients of Stock Awards may be given an opportunity to benefit from increases in value of the Common Stock through the granting of the following Stock Awards: (i) Incentive Stock Options, (ii) Nonstatutory Stock Options, (iii) stock bonuses and (iv) rights to acquire restricted stock.

(d) The Company, by means of the Plan, seeks to retain the services of the group of persons eligible to receive Stock Awards, to secure and retain the services of new members of this group and to provide incentives for such persons to exert maximum efforts for the success of the Company and its Affiliates.

2. DEFINITIONS.

(a) "AFFILIATE" means any parent corporation or subsidiary corporation of the Company, whether now or hereafter existing, as those terms are defined in Sections 424(e) and (f), respectively, of the Code.

(b) "BOARD" means the Board of Directors of the Company.

(c) "CODE" means the Internal Revenue Code of 1986, as amended.

(d) "COMMITTEE" means a committee of one or more members of the Board appointed by the Board in accordance with subsection 3(c).

(e) "COMMON STOCK" means the common stock of the Company.

(f) "COMPANY" means Rigel Pharmaceuticals, Inc., a Delaware corporation.

(g) "CONSULTANT" means any person, including an advisor, (i) engaged by the Company or an Affiliate to render consulting or advisory services and who is compensated for

such services or (ii) who is a member of the Board of Directors of an Affiliate. However, the term "Consultant" shall not include either Directors who are not compensated by the Company for their services as Directors or Directors who are merely paid a director's fee by the Company for their services as Directors.

(h) "CONTINUOUS SERVICE" means that the Participant's service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. The Participant's Continuous Service shall not be deemed to have terminated merely because of a change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Consultant or Director or a change in the entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service. For example, a change in status without interruption from an Employee of the Company to a Consultant of an Affiliate or a Director will not constitute an interruption of Continuous Service. The Board or the chief executive officer of the Company, in that party's sole discretion, may determine whether Continuous Service shall be considered interrupted in the case of any leave of absence approved by that party, including sick leave, military leave or any other personal leave.

(i) "COVERED EMPLOYEE" means the chief executive officer and the four (4) other highest compensated officers of the Company for whom total compensation is required to be reported to Stockholders under the Exchange Act, as determined for purposes of Section 162(m) of the Code.

(j) "DIRECTOR" means a member of the Board of Directors of the Company.

(k) "DISABILITY" means the permanent and total disability of a person within the meaning of Section 22(e)(3) of the Code.

(l) "EMPLOYEE" means any person employed by the Company or an Affiliate. Mere service as a Director or payment of a director's fee by the Company or an Affiliate shall not be sufficient to constitute "employment" by the Company or an Affiliate.

(m) "EXCHANGE ACT" means the Securities Exchange Act of 1934, as amended.

(n) "FAIR MARKET VALUE" means, as of any date, the value of the Common Stock determined as follows:

(i) If the Common Stock is listed on any established stock exchange or traded on the Nasdaq National Market or the Nasdaq SmallCap Market, the Fair Market Value of a share of Common Stock shall be the closing sales price for such stock (or the closing bid, if no sales were reported) as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Common Stock) on the last market trading day prior to the day of determination, as reported in THE WALL STREET JOURNAL or such other source as the Board deems reliable.

(ii) In the absence of such markets for the Common Stock, the Fair Market Value shall be determined in good faith by the Board.

(o) "INCENTIVE STOCK OPTION" means an Option intended to qualify as an incentive stock option within the meaning of Section 422 of the Code and the regulations promulgated thereunder.

(p) "NON-EMPLOYEE DIRECTOR" means a Director who either (i) is not a current Employee or Officer of the Company or its parent or a subsidiary, does not receive compensation (directly or indirectly) from the Company or its parent or a subsidiary for services rendered as a consultant or in any capacity other than as a Director (except for an amount as to which disclosure would not be required under Item 404(a) of Regulation S-K promulgated pursuant to the Securities Act ("Regulation S-K")), does not possess an interest in any other transaction as to which disclosure would be required under Item 404(a) of Regulation S-K and is not engaged in a business relationship as to which disclosure would be required under Item 404(b) of Regulation S-K; or (ii) is otherwise considered a "non-employee director" for purposes of Rule 16b-3.

(q) "NONSTATUTORY STOCK OPTION" means an Option not intended to qualify as an Incentive Stock Option.

(r) "OFFICER" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act and the rules and regulations promulgated thereunder.

(s) "OPTION" means an Incentive Stock Option or a Nonstatutory Stock Option granted pursuant to the Plan.

(t) "OPTION AGREEMENT" means a written agreement between the Company and an Optionholder evidencing the terms and conditions of an individual Option grant. Each Option Agreement shall be subject to the terms and conditions of the Plan.

(u) "OPTIONHOLDER" means a person to whom an Option is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Option.

(v) "OUTSIDE DIRECTOR" means a Director who either (i) is not a current employee of the Company or an "affiliated corporation" (within the meaning of Treasury Regulations promulgated under Section 162(m) of the Code), is not a former employee of the Company or an "affiliated corporation" receiving compensation for prior services (other than benefits under a tax qualified pension plan), was not an officer of the Company or an "affiliated corporation" at any time and is not currently receiving direct or indirect remuneration from the Company or an "affiliated corporation" for services in any capacity other than as a Director or (ii) is otherwise considered an "outside director" for purposes of Section 162(m) of the Code.

(w) "PARTICIPANT" means a person to whom a Stock Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Stock Award.

(x) "PLAN" means this Rigel Pharmaceuticals, Inc. 2000 Equity Incentive Plan.

(y) "RULE 16b-3" means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.

(z) "SECURITIES ACT" means the Securities Act of 1933, as amended.

(aa) "STOCK AWARD" means any right granted under the Plan, including an Option, a stock bonus and a right to acquire restricted stock.

(bb) "STOCK AWARD AGREEMENT" means a written agreement between the Company and a holder of a Stock Award evidencing the terms and conditions of an individual Stock Award grant. Each Stock Award Agreement shall be subject to the terms and conditions of the Plan.

(cc) "TEN PERCENT STOCKHOLDER" means a person who owns (or is deemed to own pursuant to Section 424(d) of the Code) stock possessing more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or of any of its Affiliates.

3. ADMINISTRATION.

(a) ADMINISTRATION BY BOARD. The Board shall administer the Plan unless and until the Board delegates administration to a Committee, as provided in subsection 3(c).

(b) POWERS OF BOARD. The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine from time to time which of the persons eligible under the Plan shall be granted Stock Awards; when and how each Stock Award shall be granted; what type or combination of types of Stock Award shall be granted; the provisions of each Stock Award granted (which need not be identical), including the time or times when a person shall be permitted to receive Common Stock pursuant to a Stock Award; and the number of shares of Common Stock with respect to which a Stock Award shall be granted to each such person.

(ii) To construe and interpret the Plan and Stock Awards granted under it, and to establish, amend and revoke rules and regulations for its administration. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Stock Award Agreement, in a manner and to the extent it shall deem necessary or expedient to make the Plan fully effective.

(iii) To amend the Plan or a Stock Award as provided in Section 12.

(iv) To terminate or suspend the Plan as provided in Section 13.

(v) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company which are not in conflict with the provisions of the Plan.

(c) DELEGATION TO COMMITTEE.

(i) GENERAL. The Board may delegate administration of the Plan to a Committee or Committees of one (1) or more members of the Board, and the term "Committee" shall apply to any person or persons to whom such authority has been delegated. If administration is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board, including the power to delegate to a subcommittee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board shall thereafter be to the Committee or subcommittee), subject, however, to such resolutions, not inconsistent with the provisions of the Plan, as may be adopted from time to time by the Board. The Board may abolish the Committee at any time and revest in the Board the administration of the Plan.

(ii) COMMITTEE COMPOSITION WHEN COMMON STOCK IS PUBLICLY TRADED. At such time as the Common Stock is publicly traded, in the discretion of the Board, a Committee may consist solely of two or more Outside Directors, in accordance with Section 162(m) of the Code, and/or solely of two or more Non-Employee Directors, in accordance with Rule 16b-3. Within the scope of such authority, the Board or the Committee may (1) delegate to a committee of one or more members of the Board who are not Outside Directors the authority to grant Stock Awards to eligible persons who are either (a) not then Covered Employees and are not expected to be Covered Employees at the time of recognition of income resulting from such Stock Award or (b) not persons with respect to whom the Company wishes to comply with Section 162(m) of the Code and/or) (2) delegate to a committee of one or more members of the Board who are not Non-Employee Directors the authority to grant Stock Awards to eligible persons who are not then subject to Section 16 of the Exchange Act.

(d) EFFECT OF BOARD'S DECISION. All determinations, interpretations and

constructions made by the Board in good faith shall not be subject to review by any person and shall be final, binding and conclusive on all persons.

4. SHARES SUBJECT TO THE PLAN.

(a) SHARE RESERVE. Subject to the provisions of Section 11 relating to adjustments upon changes in Common Stock, the Common Stock that may be issued pursuant to Stock Awards shall not exceed in the aggregate nine million five hundred twenty-five thousand (9,525,000) shares of Common Stock.

(b) REVERSION OF SHARES TO THE SHARE RESERVE. If any Stock Award shall for any reason expire or otherwise terminate, in whole or in part, without having been exercised in full, the shares of Common Stock not acquired under such Stock Award shall revert to and again become available for issuance under the Plan.

(c) SOURCE OF SHARES. The shares of Common Stock subject to the Plan may be unissued shares or reacquired shares, bought on the market or otherwise.

5. ELIGIBILITY.

(a) ELIGIBILITY FOR SPECIFIC STOCK AWARDS. Incentive Stock Options may be granted only to Employees. Stock Awards other than Incentive Stock Options may be granted to Employees, Directors and Consultants.

(b) TEN PERCENT STOCKHOLDERS. A Ten Percent Stockholder shall not be granted an Incentive Stock Option unless the exercise price of such Option is at least one hundred ten percent (110%) of the Fair Market Value of the Common Stock at the date of grant and the Option is not exercisable after the expiration of five (5) years from the date of grant.

(c) SECTION 162(m) LIMITATION. Subject to the provisions of Section 11 relating to adjustments upon changes in the shares of Common Stock, no Employee shall be eligible to be granted Options covering more than one million five hundred thousand (1,500,000) shares of Common Stock during any calendar year.

(d) CONSULTANTS.

(i) A Consultant shall not be eligible for the grant of a Stock Award if, at the time of grant, a Form S-8 Registration Statement under the Securities Act ("Form S-8") is not available to register either the offer or the sale of the Company's securities to such Consultant because of the nature of the services that the Consultant is providing to the Company, or because the Consultant is not a natural person, or as otherwise provided by the rules governing the use of Form S-8, unless the Company determines both (i) that such grant (A) shall be registered in another manner under the Securities Act (E.G., on a Form S-3 Registration Statement) or (B) does not require registration under the Securities Act in order to comply with the requirements of the Securities Act, if applicable, and (ii) that such grant complies with the securities laws of all other relevant jurisdictions.

(ii) Form S-8 generally is available to consultants and advisors only if (i) they are natural persons; (ii) they provide bona fide services to the issuer, its parents, its majority-owned subsidiaries or majority-owned subsidiaries of the issuer's parent; and (iii) the services are not in connection with the offer or sale of securities in a capital-raising transaction, and do not directly or indirectly promote or maintain a market for the issuer's securities.

6. OPTION PROVISIONS.

Each Option shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. All Options shall be separately designated Incentive Stock Options or Nonstatutory Stock Options at the time of grant, and, if certificates are issued, a separate certificate or certificates will be issued for shares of Common Stock purchased on exercise of each type of Option. The provisions of separate Options need not be identical, but each Option shall include (through incorporation of provisions hereof by reference in the Option or otherwise) the substance of each of the following provisions:

(a) TERM. Subject to the provisions of subsection 5(b) regarding Ten Percent Stockholders, no Incentive Stock Option shall be exercisable after the expiration of ten (10) years from the date it was granted.

(b) EXERCISE PRICE OF AN INCENTIVE STOCK OPTION. Subject to the provisions of subsection 5(b) regarding Ten Percent Stockholders, the exercise price of each Incentive Stock Option shall be not less than one hundred percent (100%) of the Fair Market Value of the Common Stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, an Incentive Stock

Option may be granted with an exercise price lower than that set forth in the preceding sentence if such Option is granted pursuant to an assumption or substitution for another option in a manner satisfying the provisions of Section 424(a) of the Code.

(c) EXERCISE PRICE OF A NONSTATUTORY STOCK OPTION. The exercise price of each Nonstatutory Stock Option shall be not less than eighty-five percent (85%) of the Fair Market Value of the Common Stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, a Nonstatutory Stock Option may be granted with an exercise price lower than that set forth in the preceding sentence if such Option is granted pursuant to an assumption or substitution for another option in a manner satisfying the provisions of Section 424(a) of the Code.

(d) CONSIDERATION. The purchase price of Common Stock acquired pursuant to an Option shall be paid, to the extent permitted by applicable statutes and regulations, either (i) in cash at the time the Option is exercised or (ii) at the discretion of the Board (1) by delivery to the Company of other Common Stock, (2) according to a deferred payment or other similar arrangement with the Optionholder or (3) in any other form of legal consideration that may be acceptable to the Board. Unless otherwise specifically provided in the Option, the purchase price of Common Stock acquired pursuant to an Option that is paid by delivery to the Company of other Common Stock acquired, directly or indirectly from the Company, shall be paid only by shares of the Common Stock of the Company that have been held for more than six (6) months (or such longer or shorter period of time required to avoid a charge to the Company's earnings for financial accounting purposes). At any time that the Company is incorporated in Delaware, payment of the Common Stock's "par value," as defined in the Delaware General Corporation Law, shall not be made by deferred payment.

In the case of any deferred payment arrangement, interest shall be compounded at least annually and shall be charged at the minimum rate of interest necessary to avoid the treatment as interest, under any applicable provisions of the Code, of any amounts other than amounts stated to be interest under the deferred payment arrangement.

(e) TRANSFERABILITY OF AN INCENTIVE STOCK OPTION. An Incentive Stock Option shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Optionholder only by the Optionholder. Notwithstanding the foregoing, the Optionholder may, by delivering written notice to the Company, in a form satisfactory to the Company, designate a third party who, in the event of the death of the Optionholder, shall thereafter be entitled to exercise the Option.

(f) TRANSFERABILITY OF A NONSTATUTORY STOCK OPTION. A Nonstatutory Stock Option shall be transferable to the extent provided in the Option Agreement. If the Nonstatutory Stock Option does not provide for transferability, then the Nonstatutory Stock Option shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Optionholder only by the Optionholder. Notwithstanding the foregoing, the Optionholder may, by delivering written notice to the Company, in a form satisfactory to the Company, designate a third party who, in the event of the death of the Optionholder, shall thereafter be entitled to exercise the Option.

(g) VESTING GENERALLY. The total number of shares of Common Stock subject to an Option may, but need not, vest and therefore become exercisable in periodic installments that may, but need not, be equal. The Option may be subject to such other terms and conditions on the time or times when it may be exercised (which may be based on performance or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options may vary. The provisions of this subsection 6(g) are subject to any Option provisions governing the minimum number of shares of Common Stock as to which an Option may be exercised.

(h) TERMINATION OF CONTINUOUS SERVICE. In the event an Optionholder's Continuous Service terminates (other than upon the Optionholder's death or Disability), the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise such Option as of the date of termination) but only within such period of time ending on the earlier of (i) the date three (3) months following the termination of the Optionholder's Continuous Service (or such longer or shorter period specified in the Option Agreement), or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination, the Optionholder does not exercise his or her Option within the time specified in the Option Agreement, the Option shall terminate.

(i) EXTENSION OF TERMINATION DATE. An Optionholder's Option Agreement may also provide that if the exercise of the Option following the termination of the Optionholder's Continuous Service (other than upon the Optionholder's death or Disability) would be prohibited at any time solely because the issuance of shares of Common Stock would violate the registration requirements under the

Securities Act, then the Option shall terminate on the earlier of (i) the expiration of the term of the Option set forth in the Option Agreement or (ii) the expiration of a period of three (3) months after the termination of the Optionholder's Continuous Service during which the exercise of the Option would not be in violation of such registration requirements.

(j) DISABILITY OF OPTIONHOLDER. In the event that an Optionholder's Continuous Service terminates as a result of the Optionholder's Disability, the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise such Option as of the date of termination), but only within such period of time ending on the earlier of (i) the date twelve (12) months following such termination (or such longer or shorter period specified in the Option Agreement) or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination, the Optionholder does not exercise his or her Option within the time specified herein, the Option shall terminate.

(k) DEATH OF OPTIONHOLDER. In the event (i) an Optionholder's Continuous Service terminates as a result of the Optionholder's death or (ii) the Optionholder dies within the period (if any) specified in the Option Agreement after the termination of the Optionholder's Continuous Service for a reason other than death, then the Option may be exercised (to the extent the Optionholder was entitled to exercise such Option as of the date of death) by the Optionholder's estate, by a person who acquired the right to exercise the Option by bequest or inheritance or by a person designated to exercise the Option upon the Optionholder's death pursuant to subsection 6(e) or 6(f), but only within the period ending on the earlier of (1) the date eighteen (18) months following the date of death (or such longer or shorter period specified in the Option Agreement) or (2) the expiration of the term of such Option as set forth in the Option Agreement. If, after death, the Option is not exercised within the time specified herein, the Option shall terminate.

(l) EARLY EXERCISE. The Option may, but need not, include a provision whereby the Optionholder may elect at any time before the Optionholder's Continuous Service terminates to exercise the Option as to any part or all of the shares of Common Stock subject to the Option prior to the full vesting of the Option. Any unvested shares of Common Stock so purchased may be subject to a repurchase option in favor of the Company or to any other restriction the Board determines to be appropriate. The Company will not exercise its repurchase option until at least six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes) have elapsed following exercise of the Option unless the Board otherwise specifically provides in the Option.

(m) RE-LOAD OPTIONS.

(i) Without in any way limiting the authority of the Board to make or not to make grants of Options hereunder, the Board shall have the authority (but not an obligation) to include as part of any Option Agreement a provision entitling the Optionholder to a further Option (a "Re-Load Option") in the event the Optionholder exercises the Option evidenced by the Option Agreement, in whole or in part, by surrendering other shares of Common Stock in accordance with this Plan and the terms and conditions of the Option Agreement. Unless otherwise specifically provided in the Option, the Optionholder shall not surrender shares of Common Stock acquired, directly or indirectly from the Company, unless such shares have been held for more than six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes).

(ii) Any such Re-Load Option shall (1) provide for a number of shares of Common Stock equal to the number of shares of Common Stock surrendered as part or all of the exercise price of such Option; (2) have an expiration date which is the same as the expiration date of the Option the exercise of which gave rise to such Re-Load Option; and (3) have an exercise price which is equal to one hundred percent (100%) of the Fair Market Value of the Common Stock subject to the Re-Load Option on the date of exercise of the original Option. Notwithstanding the foregoing, a Re-Load Option shall be subject to the same exercise price and term provisions heretofore described for Options under the Plan.

(iii) Any such Re-Load Option may be an Incentive Stock Option or a Nonstatutory Stock Option, as the Board may designate at the time of the grant of the original Option; PROVIDED, HOWEVER, that the designation of any Re-Load Option as an Incentive Stock Option shall be subject to the one hundred thousand dollar ($100,000) annual limitation on the exercisability of Incentive Stock Options described in subsection 10(d) and in Section 422(d) of the Code. There shall be no Re-Load Options on a Re-Load Option. Any such Re-Load Option shall be subject to the availability of sufficient shares of Common Stock under subsection 4(a) and the "Section 162(m) Limitation" on the grants of Options

under subsection 5(c) and shall be subject to such other terms and conditions as the Board may determine which are not inconsistent with the express provisions of the Plan regarding the terms of Options.

7. PROVISIONS OF STOCK AWARDS OTHER THAN OPTIONS.

(a) STOCK BONUS AWARDS. Each stock bonus agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of stock bonus agreements may change from time to time, and the terms and conditions of separate stock bonus agreements need not be identical, but each stock bonus agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) CONSIDERATION. A stock bonus may be awarded in consideration for past services actually rendered to the Company or an Affiliate for its benefit.

(ii) VESTING. Shares of Common Stock awarded under the stock bonus agreement may, but need not, be subject to a share repurchase option in favor of the Company in accordance with a vesting schedule to be determined by the Board.

(iii) TERMINATION OF PARTICIPANT'S CONTINUOUS SERVICE. In the event a Participant's Continuous Service terminates, the Company may reacquire any or all of the shares of Common Stock held by the Participant which have not vested as of the date of termination under the terms of the stock bonus agreement.

(iv) TRANSFERABILITY. Rights to acquire shares of Common Stock under the stock bonus agreement shall be transferable by the Participant only upon such terms and conditions as are set forth in the stock bonus agreement, as the Board shall determine in its discretion, so long as Common Stock awarded under the stock bonus agreement remains subject to the terms of the stock bonus agreement.

(b) RESTRICTED STOCK AWARDS. Each restricted stock purchase agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of the restricted stock purchase agreements may change from time to time, and the terms and conditions of separate restricted stock purchase agreements need not be identical, but each restricted stock purchase agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) PURCHASE PRICE. The purchase price under each restricted stock purchase agreement shall be such amount as the Board shall determine and designate in such restricted stock purchase agreement. The purchase price shall not be less than eighty-five percent (85%) of the Common Stock's Fair Market Value on the date such award is made or at the time the purchase is consummated.

(ii) CONSIDERATION. The purchase price of Common Stock acquired pursuant to the restricted stock purchase agreement shall be paid either: (i) in cash at the time of purchase; (ii) at the discretion of the Board, according to a deferred payment or other similar arrangement with the Participant; or (iii) in any other form of legal consideration that may be acceptable to the Board in its discretion; PROVIDED, HOWEVER, that at any time that the Company is incorporated in Delaware, then payment of the Common Stock's "par value," as defined in the Delaware General Corporation Law, shall not be made by deferred payment.

(iii) VESTING. Shares of Common Stock acquired under the restricted stock purchase agreement may, but need not, be subject to a share repurchase option in favor of the Company in accordance with a vesting schedule to be determined by the Board.

(iv) TERMINATION OF PARTICIPANT'S CONTINUOUS SERVICE. In the event a Participant's Continuous Service terminates, the Company may repurchase or otherwise reacquire any or all of the shares of Common Stock held by the Participant which have not vested as of the date of termination under the terms of the restricted stock purchase agreement.

(v) TRANSFERABILITY. Rights to acquire shares of Common Stock under the restricted stock purchase agreement shall be transferable by the Participant only upon such terms and conditions as are set forth in the restricted stock purchase agreement, as the Board shall determine in its discretion, so long as Common Stock awarded under the restricted stock purchase agreement remains subject to the terms of the restricted stock purchase agreement.

8. COVENANTS OF THE COMPANY.

(a) AVAILABILITY OF SHARES. During the terms of the Stock Awards, the Company shall keep available at all times the number of shares of Common Stock required to satisfy such Stock Awards.

(b) SECURITIES LAW COMPLIANCE. The Company shall seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell shares of Common Stock upon exercise of the Stock Awards; PROVIDED, HOWEVER, that this undertaking shall not require the Company to register under the Securities Act the Plan, any Stock Award or any Common Stock issued or issuable pursuant to any such Stock Award. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority which counsel for the Company deems necessary for the lawful issuance and sale of Common Stock under the Plan, the Company shall be relieved from any liability for failure to issue and sell Common Stock upon exercise of such Stock Awards unless and until such authority is obtained.

9. USE OF PROCEEDS FROM STOCK.

Proceeds from the sale of Common Stock pursuant to Stock Awards shall constitute general funds of the Company.

10. MISCELLANEOUS.

(a) ACCELERATION OF EXERCISABILITY AND VESTING. The Board shall have the power to accelerate the time at which a Stock Award may first be exercised or the time during which a Stock Award or any part thereof will vest in accordance with the Plan, notwithstanding the provisions in the Stock Award stating the time at which it may first be exercised or the time during which it will vest.

(b) STOCKHOLDER RIGHTS. No Participant shall be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Common Stock subject to such Stock Award unless and until such Participant has satisfied all requirements for exercise of the Stock Award pursuant to its terms.

(c) NO EMPLOYMENT OR OTHER SERVICE RIGHTS. Nothing in the Plan or any instrument executed or Stock Award granted pursuant thereto shall confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Stock Award was granted or shall affect the right of the Company or an Affiliate to terminate (i) the employment of an Employee with or without notice and with or without cause, (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or an Affiliate or (iii) the service of a Director pursuant to the Bylaws of the Company or an Affiliate, and any applicable provisions of the corporate law of the state in which the Company or the Affiliate is incorporated, as the case may be.

(d) INCENTIVE STOCK OPTION $100,000 LIMITATION. To the extent that the aggregate Fair Market Value (determined at the time of grant) of Common Stock with respect to which Incentive Stock Options are exercisable for the first time by any Optionholder during any calendar year (under all plans of the Company and its Affiliates) exceeds one hundred thousand dollars ($100,000), the Options or portions thereof which exceed such limit (according to the order in which they were granted) shall be treated as Nonstatutory Stock Options.

(e) INVESTMENT ASSURANCES. The Company may require a Participant, as a condition of exercising or acquiring Common Stock under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Stock Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Common Stock subject to the Stock Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Common Stock. The foregoing requirements, and any assurances given pursuant to such requirements, shall be inoperative if (1) the issuance of the shares of Common Stock

upon the exercise or acquisition of Common Stock under the Stock Award has been registered under a then currently effective registration statement under the Securities Act or (2) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on stock certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply

with applicable securities laws, including, but not limited to, legends restricting the transfer of the Common Stock.

(f) WITHHOLDING OBLIGATIONS. To the extent provided by the terms of a Stock Award Agreement, the Participant may satisfy any federal, state or local tax withholding obligation relating to the exercise or acquisition of Common Stock under a Stock Award by any of the following means (in addition to the Company's right to withhold from any compensation paid to the Participant by the Company) or by a combination of such means: (i) tendering a cash payment; (ii) authorizing the Company to withhold shares of Common Stock from the shares of Common Stock otherwise issuable to the Participant as a result of the exercise or acquisition of Common Stock under the Stock Award, PROVIDED, HOWEVER, that no shares of Common Stock are withheld with a value exceeding the minimum amount of tax required to be withheld by law; or (iii) delivering to the Company owned and unencumbered shares of Common Stock of the Company that have been held for more than six (6) months (or such longer or shorter period of time required to avoid a charge to the Company's earnings for financial accounting purposes).

11. ADJUSTMENTS UPON CHANGES IN STOCK.

(a) CAPITALIZATION ADJUSTMENTS. If any change is made in the Common Stock subject to the Plan, or subject to any Stock Award, without the receipt of consideration by the Company (through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other transaction not involving the receipt of consideration by the Company), the Plan will be appropriately adjusted in the class(es) and maximum number of securities subject to the Plan pursuant to subsection 4(a) and the maximum number of securities subject to award to any person pursuant to subsection 5(c), and the outstanding Stock Awards will be appropriately adjusted in the class(es) and number of securities and price per share of Common Stock subject to such outstanding Stock Awards. The Board shall make such adjustments, and its determination shall be final, binding and conclusive. (The conversion of any convertible securities of the Company shall not be treated as a transaction "without receipt of consideration" by the Company.)

(b) DISSOLUTION OR LIQUIDATION. In the event of a dissolution or liquidation of the Company, then all outstanding Stock Awards shall terminate immediately prior to such event. Notwithstanding the foregoing, Options granted under the 1997 Stock Option Plan shall be subject to Section 11(c) below in the event of a dissolution or liquidation of the Company.

(c) CHANGE IN CONTROL. In the event of (i) a sale, lease or other disposition of all or substantially all of the securities or assets of the Company, (ii) a merger or consolidation in which the Company is not the surviving corporation or (iii) a reverse merger in which the

Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise, then any surviving corporation or acquiring corporation may assume any Stock Awards outstanding under the Plan or may substitute similar stock awards (including an award to acquire the same consideration paid to the Stockholders in the transaction described in this subsection 11(c)) for those outstanding under the Plan. In the event any surviving corporation or acquiring corporation does not assume such Stock Awards or substitute similar stock awards for those outstanding under the Plan, then with respect to Stock Awards held by Participants whose Continuous Service has not terminated, the vesting of such Stock Awards (and, if applicable, the time during which such Stock Awards may be exercised) shall be accelerated in full, and the Stock Awards shall terminate if not exercised (if applicable) at or prior to such event. With respect to any other Stock Awards outstanding under the Plan, such Stock Awards shall terminate if not exercised (if applicable) prior to such event.

12. AMENDMENT OF THE PLAN AND STOCK AWARDS.

(a) AMENDMENT OF PLAN. The Board at any time, and from time to time, may amend the Plan. However, except as provided in Section 11 relating to adjustments upon changes in Common Stock, no amendment shall be effective unless approved by the Stockholders of the Company to the extent Stockholder approval is necessary to satisfy the requirements of Section 422 of the Code, Rule 16b-3 or any Nasdaq or securities exchange listing requirements.

(b) STOCKHOLDER APPROVAL. The Board may, in its sole discretion, submit any other amendment to the Plan for Stockholder approval, including, but not limited to, amendments to the Plan intended to satisfy the requirements of Section 162(m) of the Code and the regulations thereunder regarding the exclusion of performance-based compensation from the limit on corporate deductibility of compensation paid to certain executive officers.

(c) CONTEMPLATED AMENDMENTS. It is expressly contemplated that the

Board may amend the Plan in any respect the Board deems necessary or advisable to provide eligible Employees with the maximum benefits provided or to be provided under the provisions of the Code and the regulations promulgated thereunder relating to Incentive Stock Options and/or to bring the Plan and/or Incentive Stock Options granted under it into compliance therewith.

(d) NO IMPAIRMENT OF RIGHTS. Rights under any Stock Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (i) the Company requests the consent of the Participant and (ii) the Participant consents in writing.

(e) AMENDMENT OF STOCK AWARDS. The Board at any time, and from time to time, may amend the terms of any one or more Stock Awards; PROVIDED, HOWEVER, that the rights under any Stock Award shall not be impaired by any such amendment unless (i) the Company requests the consent of the Participant and (ii) the Participant consents in writing.

13. TERMINATION OR SUSPENSION OF THE PLAN.

(a) PLAN TERM. The Board may suspend or terminate the Plan at any time. Unless sooner terminated, the Plan shall terminate on the day before the tenth (10th) anniversary of the date the Plan is approved by the stockholders of the Company. No Stock Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) NO IMPAIRMENT OF RIGHTS. Suspension or termination of the Plan shall not impair rights and obligations under any Stock Award granted while the Plan is in effect except with the written consent of the Participant.

14. EFFECTIVE DATE OF PLAN.

The Plan shall become effective upon its adoption by the Board, but no Stock Award shall be exercised (or, in the case of a stock bonus, shall be granted) unless and until the Plan has been approved by the Stockholders of the Company, which approval shall be within twelve (12) months before or after the date the Plan is adopted by the Board.

15. CHOICE OF LAW.

The law of the State of Delaware shall govern all questions concerning the construction, validity and interpretation of this Plan, without regard to such state's conflict of laws rules.

EXHIBIT 10.3

RIGEL PHARMACEUTICALS, INC.
2000 EQUITY INCENTIVE PLAN

STOCK OPTION AGREEMENT
(INCENTIVE AND NONSTATUTORY STOCK OPTIONS)

Pursuant to your Stock Option Grant Notice ("Grant Notice") and this Stock Option Agreement, RIGEL PHARMACEUTICALS, INC. (the "Company") has granted you an option under its 2000 EQUITY INCENTIVE PLAN (the "Plan") to purchase the number of shares of the Company's Common Stock indicated in your Grant Notice at the exercise price indicated in your Grant Notice. Defined terms not explicitly defined in this Stock Option Agreement but defined in the Plan shall have the same definitions as in the Plan.

The details of your option are as follows:

1. VESTING. Subject to the limitations contained herein, your option will vest as provided in your Grant Notice, provided that vesting will cease upon the termination of your Continuous Service.

2. NUMBER OF SHARES AND EXERCISE PRICE. The number of shares of Common Stock subject to your option and your exercise price per share referenced in your Grant Notice may be adjusted from time to time for Capitalization Adjustments, as provided in the Plan.

3. EXERCISE PRIOR TO VESTING ("EARLY EXERCISE"). If permitted in your Grant Notice (i.e., the "Exercise Schedule" indicates that "Early Exercise" of your option is permitted) and subject to the provisions of your option, you may elect at any time that is both (i) during the period of your Continuous Service and (ii) during the term of your option, to exercise all or part of your option, including the nonvested portion of your option; provided, however, that:

(a) a partial exercise of your option shall be deemed to cover first vested shares of Common Stock and then the earliest vesting installment of unvested shares of Common Stock;

(b) any shares of Common Stock so purchased from installments that have not vested as of the date of exercise shall be subject to the purchase option in favor of the Company as described in the Company's form of Early Exercise Stock Purchase Agreement;

(c) you shall enter into the Company's form of Early Exercise Stock Purchase Agreement with a vesting schedule that will result in the same vesting as if no early exercise had occurred; and

(d) if your option is an incentive stock option, then, as provided in the Plan, to the extent that the aggregate Fair Market Value (determined at the time of grant) of the shares of Common Stock with respect to which your option plus all other incentive stock options you hold are exercisable for the first time by you during any calendar year (under all plans of the

Company and its Affiliates) exceeds one hundred thousand dollars ($100,000), your option(s) or portions thereof that exceed such limit (according to the order in which they were granted) shall be treated as nonstatutory stock options.

4. METHOD OF PAYMENT. Payment of the exercise price is due in full upon exercise of all or any part of your option. You may elect to make payment of the exercise price in cash or by check or in any other manner PERMITTED BY YOUR GRANT NOTICE, which may include one or more of the following:

(a) In the Company's sole discretion at the time your option is exercised and provided that at the time of exercise the Common Stock is publicly traded and quoted regularly in THE WALL STREET JOURNAL, pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board that, prior to the issuance of Common Stock, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds.

(b) Provided that at the time of exercise the Common Stock is publicly traded and quoted regularly in THE WALL STREET JOURNAL, by delivery of already-owned shares of Common Stock either that you have held for the period required to avoid a charge to the Company's reported earnings (generally six months) or that you did not acquire, directly or indirectly from the Company, that are owned free and clear of any liens, claims, encumbrances or security interests, and that are valued at Fair Market Value on the date of exercise. "Delivery" for these purposes, in the sole discretion of the Company at the time

you exercise your option, shall include delivery to the Company of your attestation of ownership of such shares of Common Stock in a form approved by the Company. Notwithstanding the foregoing, you may not exercise your option by tender to the Company of Common Stock to the extent such tender would violate the provisions of any law, regulation or agreement restricting the redemption of the Company's stock.

5. WHOLE SHARES. You may exercise your option only for whole shares of Common Stock.

6. SECURITIES LAW COMPLIANCE. Notwithstanding anything to the contrary contained herein, you may not exercise your option unless the shares of Common Stock issuable upon such exercise are then registered under the Securities Act or, if such shares of Common Stock are not then so registered, the Company has determined that such exercise and issuance would be exempt from the registration requirements of the Securities Act. The exercise of your option must also comply with other applicable laws and regulations governing your option, and you may not exercise your option if the Company determines that such exercise would not be in material compliance with such laws and regulations.

7. TERM. You may not exercise your option before the commencement of its term or after its term expires. The term of your option commences on the Date of Grant and expires upon the EARLIEST of the following:

(a) immediately upon the termination of your Continuous Service for Cause;

(b) three (3) months after the termination of your Continuous Service for any reason other than Cause, Disability or death, provided that if during any part of such three- (3-) month period you may not exercise your option solely because of the condition set forth in the preceding paragraph relating to "Securities Law Compliance," your option shall not expire until the earlier of the Expiration Date or until it shall have been exercisable for an aggregate period of three (3) months after the termination of your Continuous Service;

(c) twelve (12) months after the termination of your Continuous Service due to your Disability;

(d) eighteen (18) months after your death if you die either during your Continuous Service or within three (3) months after your Continuous Service terminates for reason other than Cause;

(e) the Expiration Date indicated in your Grant Notice; or

(f) the day before the tenth (10th) anniversary of the Date of Grant.

For purposes of your option, "Cause" means your misconduct, including but not limited to: (i) your conviction of any felony or any crime involving moral turpitude or dishonesty, (ii) your participation in a fraud or act of dishonesty against the Company, (iii) your conduct that, based upon a good faith and reasonable factual investigation and determination by the Board, demonstrates your gross unfitness to serve, or (iv) your intentional, material violation of any contract between the Company and you or any statutory duty of yours to the Company that you do not correct within thirty (30) days after written notice to you thereof. Your physical or mental disability shall not constitute "Cause."

If your option is an incentive stock option, note that, to obtain the federal income tax advantages associated with an "incentive stock option," the Code requires that at all times beginning on the date of grant of your option and ending on the day three (3) months before the date of your option's exercise, you must be an employee of the Company or an Affiliate, except in the event of your death or Disability. The Company has provided for extended exercisability of your option under certain circumstances for your benefit but cannot guarantee that your option will necessarily be treated as an "incentive stock option" if you continue to provide services to the Company or an Affiliate as a Consultant or Director after your employment terminates or if you otherwise exercise your option more than three (3) months after the date your employment terminates.

8. EXERCISE.

(a) You may exercise the vested portion of your option (and the unvested portion of your option if your Grant Notice so permits) during its term by delivering a Notice of Exercise (in a form designated by the Company) together with the exercise price to the Secretary of the Company, or to such other person as the Company may designate, during regular business hours, together with such additional documents as the Company may then require.

(b) By exercising your option you agree that, as a condition to any exercise of your option, the Company may require you to enter into an arrangement providing for the payment by you to the Company of any tax withholding obligation of the Company arising by reason of (1) the exercise of your option, (2) the lapse of any substantial risk of forfeiture to which the shares of Common Stock are subject at the time of exercise, or (3) the disposition of shares of Common Stock acquired upon such exercise.

(c) If your option is an incentive stock option, by exercising your option you agree that you will notify the Company in writing within fifteen (15) days after the date of any disposition of any of the shares of the Common Stock issued upon exercise of your option that occurs within two (2) years after the date of your option grant or within one (1) year after such shares of Common Stock are transferred upon exercise of your option.

9. TRANSFERABILITY. Your option is not transferable, except by will or by the laws of descent and distribution, and is exercisable during your life only by you. Notwithstanding the foregoing, by delivering written notice to the Company, in a form satisfactory to the Company, you may designate a third party who, in the event of your death, shall thereafter be entitled to exercise your option.

10. OPTION NOT A SERVICE CONTRACT. Your option is not an employment or service contract, and nothing in your option shall be deemed to create in any way whatsoever any obligation on your part to continue in the employ of the Company or an Affiliate, or of the Company or an Affiliate to continue your employment. In addition, nothing in your option shall obligate the Company or an Affiliate, their respective shareholders, Boards of Directors, Officers or Employees to continue any relationship that you might have as a Director or Consultant for the Company or an Affiliate.

11. WITHHOLDING OBLIGATIONS.

(a) At the time you exercise your option, in whole or in part, or at any time thereafter as requested by the Company, you hereby authorize withholding from payroll and any other amounts payable to you, and otherwise agree to make adequate provision for (including by means of a "cashless exercise" pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board to the extent permitted by the Company), any sums required to satisfy the federal, state, local and foreign tax withholding obligations of the Company or an Affiliate, if any, which arise in connection with your option.

(b) Upon your request and subject to approval by the Company, in its sole discretion, and compliance with any applicable conditions or restrictions of law, the Company may withhold from fully vested shares of Common Stock otherwise issuable to you upon the exercise of your option a number of whole shares of Common Stock having a Fair Market Value, determined by the Company as of the date of exercise, not in excess of the minimum amount of tax required to be withheld by law. If the date of determination of any tax withholding obligation is deferred to a date later than the date of exercise of your option, share withholding pursuant to the preceding sentence shall not be permitted unless you make a proper and timely election under Section 83(b) of the Code, covering the aggregate number of shares of Common

Stock acquired upon such exercise with respect to which such determination is otherwise deferred, to accelerate the determination of such tax withholding obligation to the date of exercise of your option. Notwithstanding the filing of such election, shares of Common Stock shall be withheld solely from fully vested shares of Common Stock determined as of the date of exercise of your option that are otherwise issuable to you upon such exercise. Any adverse consequences to you arising in connection with such share withholding procedure shall be your sole responsibility.

(c) You may not exercise your option unless the tax withholding obligations of the Company and/or any Affiliate are satisfied. Accordingly, you may not be able to exercise your option when desired even though your option is vested, and the Company shall have no obligation to issue a certificate for such shares of Common Stock or release such shares of Common Stock from any escrow provided for herein.

12. NOTICES. Any notices provided for in your option or the Plan shall be given in writing and shall be deemed effectively given upon receipt or, in the case of notices delivered by mail by the Company to you, five (5) days after deposit in the United States mail, postage prepaid, addressed to you at the last address you provided to the Company.

13. GOVERNING PLAN DOCUMENT. Your option is subject to all the provisions of the Plan, the provisions of which are hereby made a part of your option, and is further subject to all interpretations, amendments, rules and

regulations which may from time to time be promulgated and adopted pursuant to the Plan. In the event of any conflict between the provisions of your option and those of the Plan, the provisions of the Plan shall control.

EXHIBIT 10.4

RIGEL PHARMACEUTICALS, INC.

2000 EMPLOYEE STOCK PURCHASE PLAN

APPROVED BY THE BOARD OF DIRECTORS AUGUST 18, 2000
APPROVED BY STOCKHOLDERS _____, 2000

1. PURPOSE.

(a) The purpose of this 2000 Employee Stock Purchase Plan (the "Plan") is to provide a means by which employees of Rigel Pharmaceuticals, Inc. (the "Company") and its Affiliates, as defined in subparagraph 1(b), that are designated as provided in subparagraph 2(b), may be given an opportunity to purchase common stock of the Company (the "Common Stock").

(b) The word "Affiliate" as used in the Plan means any parent corporation or subsidiary corporation of the Company, as those terms are defined in Sections 424(e) and (f), respectively, of the Internal Revenue Code of 1986, as amended (the "Code").

(c) The Company, by means of the Plan, seeks to retain the services of its employees, to secure and retain the services of new employees, and to provide incentives for such persons to exert maximum efforts for the success of the Company.

(d) The Company intends that the rights to purchase stock of the Company granted under the Plan be considered options issued under an "employee stock purchase plan" as that term is defined in Section 423(b) of the Code.

2. ADMINISTRATION.

(a) The Plan shall be administered by the Board of Directors (the "Board") of the Company unless and until the Board delegates administration to a Committee, as provided in subparagraph 2(c). Whether or not the Board has delegated administration, the Board shall have the final power to determine all questions of policy and expediency that may arise in the administration of the Plan.

(b) The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine when and how rights to purchase stock of the Company shall be granted and the provisions of each offering of such rights (which need not be identical).

(ii) To designate from time to time which Affiliates of the Company shall be eligible to participate in the Plan.

(iii) To construe and interpret the Plan and rights granted under it, and to establish, amend and revoke rules and regulations for its administration. The Board, in the

exercise of this power, may correct any defect, omission or inconsistency in the Plan, in a manner and to the extent it shall deem necessary or expedient to make the Plan fully effective.

(iv) To amend the Plan as provided in paragraph 13.

(v) To terminate or suspend the Plan as provided in paragraph 15.

(vi) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and its Affiliates and to carry out the intent that the Plan be treated as an "employee stock purchase plan" within the meaning of Section 423 of the Code.

(c) The Board may delegate administration of the Plan to a Committee composed of not fewer than two (2) members of the Board (the "Committee"). If administration is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board, subject, however, to such resolutions, not inconsistent with the provisions of the Plan, as may be adopted from time to time by the Board. The Board may abolish the Committee at any time and revest in the Board the administration of the Plan.

3. SHARES SUBJECT TO THE PLAN.

(a) Subject to the provisions of paragraph 12 relating to adjustments upon changes in stock and subject to the increases in the number of reserved shares described below, the stock that may be sold pursuant to rights granted under the Plan shall not exceed in the aggregate four hundred thousand (400,000) shares of Common Stock (the "Reserved Shares"). As of the first nine (9) anniversaries of the Effective Date of the Plan, the number of Reserved Shares will be increased automatically by the LEAST of (i) one percent (1%) of the total number of shares of Common Stock outstanding on such anniversary date, (ii) four hundred thousand (400,000) shares or (iii) a number of shares determined by the Board prior to the anniversary date, which number shall be less than (i) and (ii) above. If any right granted under the Plan shall for any reason terminate without having been exercised, the Common Stock not purchased under such right shall again become available for the Plan.

(b) The stock subject to the Plan may be unissued shares or reacquired shares, bought on the market or otherwise.

4. GRANT OF RIGHTS; OFFERING.

The Board or the Committee may from time to time grant or provide for the grant of rights to purchase Common Stock of the Company under the Plan to eligible employees (an "Offering") on a date or dates (the "Offering Date(s)") selected by the Board or the Committee. Each Offering shall be in such form and shall contain such terms and conditions as the Board or the Committee shall deem appropriate, which shall comply with the requirements of Section 423(b)(5) of the Code that all employees granted rights to purchase stock under the Plan shall have the same rights and privileges. The terms and conditions of an Offering shall be

incorporated by reference into the Plan and treated as part of the Plan. The provisions of separate Offerings need not be identical, but each Offering shall include (through incorporation of the provisions of this Plan by reference in the document comprising the Offering or otherwise) the period during which the Offering shall be effective, which period shall not exceed twenty-seven (27) months beginning with the Offering Date, and the substance of the provisions contained in paragraphs 5 through 8, inclusive.

5. ELIGIBILITY.

(a) Rights may be granted only to employees of the Company or, as the Board or the Committee may designate as provided in subparagraph 2(b), to employees of any Affiliate of the Company. Except as provided in subparagraph 5(b), an employee of the Company or any Affiliate shall not be eligible to be granted rights under the Plan unless, on the Offering Date, such employee has been in the employ of the Company or any Affiliate for such continuous period preceding such grant as the Board or the Committee may require, but in no event shall the required period of continuous employment be greater than two (2) years. In addition, unless otherwise determined by the Board or the Committee and set forth in the terms of the applicable Offering, no employee of the Company or any Affiliate shall be eligible to be granted rights under the Plan, unless, on the Offering Date, such employee's customary employment with the Company or such Affiliate is for at least twenty (20) hours per week and at least five (5) months per calendar year.

(b) The Board or the Committee may provide that each person who, during the course of an Offering, first becomes an eligible employee of the Company or designated Affiliate will, on a date or dates specified in the Offering which coincides with the day on which such person becomes an eligible employee or occurs thereafter, receive a right under that Offering, which right shall thereafter be deemed to be a part of that Offering. Such right shall have the same characteristics as any rights originally granted under that Offering, as described herein, except that:

(i) the date on which such right is granted shall be the "Offering Date" of such right for all purposes, including determination of the exercise price of such right;

(ii) the period of the Offering with respect to such right shall begin on its Offering Date and end coincident with the end of such Offering; and

(iii) the Board or the Committee may provide that if such person first becomes an eligible employee within a specified period of time before the end of the Offering, he or she will not receive any right under that Offering.

(c) No employee shall be eligible for the grant of any rights under the Plan if, immediately after any such rights are granted, such employee owns stock possessing five percent (5%) or more of the total combined voting power or value of all classes of stock of the Company or of any Affiliate. For purposes of this subparagraph 5(c), the rules of Section 424(d) of the Code shall apply in determining the stock ownership of any employee, and stock which such

employee may purchase under all outstanding rights and options shall be treated as stock owned by such employee.

(d) An eligible employee may be granted rights under the Plan only if such rights, together with any other rights granted under "employee stock purchase plans" of the Company and any Affiliates, as specified by Section 423(b)(8) of the Code, do not permit such employee's rights to purchase stock of the Company or any Affiliate to accrue at a rate which exceeds twenty-five thousand dollars ($25,000) of fair market value of such stock (determined at the time such rights are granted) for each calendar year in which such rights are outstanding at any time.

(e) Officers of the Company and any designated Affiliate shall be eligible to participate in Offerings under the Plan; PROVIDED, HOWEVER, that the Board may provide in an Offering that certain employees who are highly compensated employees within the meaning of Section 423(b)(4)(D) of the Code shall not be eligible to participate.

6. RIGHTS; PURCHASE PRICE.

(a) On each Offering Date, each eligible employee, pursuant to an Offering made under the Plan, shall be granted the right to purchase up to the number of shares of Common Stock of the Company purchasable with a percentage designated by the Board or the Committee not exceeding fifteen percent (15%) of such employee's Earnings (as defined in subparagraph 7(a)) during the period which begins on the Offering Date (or such later date as the Board or the Committee determines for a particular Offering) and ends on the date stated in the Offering, which date shall be no later than the end of the Offering. The Board or the Committee shall establish one or more dates during an Offering (the "Purchase Date(s)") on which rights granted under the Plan shall be exercised and purchases of Common Stock carried out in accordance with such Offering.

(b) In connection with each Offering made under the Plan, the Board or the Committee may specify a maximum number of shares that may be purchased by any employee as well as a maximum aggregate number of shares that may be purchased by all eligible employees pursuant to such Offering. In addition, in connection with each Offering that contains more than one Purchase Date, the Board or the Committee may specify a maximum aggregate number of shares which may be purchased by all eligible employees on any given Purchase Date under the Offering. If the aggregate purchase of shares upon exercise of rights granted under the Offering would exceed any such maximum aggregate number, the Board or the Committee shall make a pro rata allocation of the shares available in as nearly a uniform manner as shall be practicable and as it shall deem to be equitable.

(c) The purchase price of stock acquired pursuant to rights granted under the Plan shall be not less than the lesser of:

(i) an amount equal to eighty-five percent (85%) of the fair market value of the stock on the Offering Date; or

(ii) an amount equal to eighty-five percent (85%) of the fair market value of the stock on the Purchase Date.

7. PARTICIPATION; WITHDRAWAL; TERMINATION.

(a) An eligible employee may become a participant in the Plan pursuant to an Offering by delivering a participation agreement to the Company within the time specified in the Offering, in such form as the Company provides. Each such agreement shall authorize payroll deductions of up to the maximum percentage specified by the Board or the Committee of such employee's Earnings during the Offering. "Earnings" is defined as an employee's wages (including amounts thereof elected to be deferred by the employee, that would otherwise have been paid, under any arrangement established by the Company that is intended to comply with Section 125, Section 401(k), Section 402(h) or Section 403(b) of the Code or that provides non-qualified deferred compensation), which shall include overtime pay, bonuses, incentive pay, and commissions, but shall exclude profit sharing or other remuneration paid directly to the employee, the cost of employee benefits paid for by the Company or an Affiliate, education or tuition reimbursements, imputed income arising under any group insurance or benefit program, traveling expenses, business and moving expense reimbursements, income received in connection with stock options, contributions made by the Company or an Affiliate under any employee benefit plan, and similar items of compensation, as determined by the Board or the Committee. The payroll deductions made for each participant shall be credited to an account for such participant under the Plan and shall be deposited with the general funds of the Company. A participant may reduce (including to zero) or increase such payroll deductions, and an eligible employee may begin such payroll deductions, after the beginning of any

Offering only as provided for in the Offering. A participant may make additional payments into his or her account only if specifically provided for in the Offering and only if the participant has not had the maximum amount withheld during the Offering.

(b) At any time during an Offering, a participant may terminate his or her payroll deductions under the Plan and withdraw from the Offering by delivering to the Company a notice of withdrawal in such form as the Company provides. Such withdrawal may be elected at any time prior to the end of the Offering except as provided by the Board or the Committee in the Offering. Upon such withdrawal from the Offering by a participant, the Company shall distribute to such participant all of his or her accumulated payroll deductions (reduced to the extent, if any, such deductions have been used to acquire stock for the participant) under the Offering, without interest, and such participant's interest in that Offering shall be automatically terminated. A participant's withdrawal from an Offering will have no effect upon such participant's eligibility to participate in any other Offerings under the Plan but such participant will be required to deliver a new participation agreement in order to participate in subsequent Offerings under the Plan.

(c) Rights granted pursuant to any Offering under the Plan shall terminate immediately upon cessation of any participating employee's employment with the Company and any designated Affiliate, for any reason, and the Company shall distribute to such terminated employee all of his or her accumulated payroll deductions (reduced to the extent, if any, such

deductions have been used to acquire stock for the terminated employee), under the Offering, without interest.

(d) Rights granted under the Plan shall not be transferable by a participant otherwise than by will or the laws of descent and distribution, or by a beneficiary designation as provided in paragraph 14 and, otherwise during his or her lifetime, shall be exercisable only by the person to whom such rights are granted.

8. EXERCISE.

(a) On each Purchase Date specified therefor in the relevant Offering, each participant's accumulated payroll deductions and other additional payments specifically provided for in the Offering (without any increase for interest) will be applied to the purchase of whole shares of stock of the Company, up to the maximum number of shares permitted pursuant to the terms of the Plan and the applicable Offering, at the purchase price specified in the Offering. No fractional shares shall be issued upon the exercise of rights granted under the Plan. The amount, if any, of accumulated payroll deductions remaining in each participant's account after the purchase of shares which is less than the amount required to purchase one share of stock on the final Purchase Date of an Offering shall be held in each such participant's account for the purchase of shares under the next Offering under the Plan, unless such participant withdraws from such next Offering, as provided in subparagraph 7(b), or is no longer eligible to be granted rights under the Plan, as provided in paragraph 5, in which case such amount shall be distributed to the participant after such final Purchase Date, without interest. The amount, if any, of accumulated payroll deductions remaining in any participant's account after the purchase of shares which is equal to the amount required to purchase whole shares of stock on the final Purchase Date of an Offering shall be distributed in full to the participant after such Purchase Date, without interest.

(b) No rights granted under the Plan may be exercised to any extent unless the shares to be issued upon such exercise under the Plan (including rights granted thereunder) are covered by an effective registration statement pursuant to the Securities Act of 1933, as amended (the "Securities Act") and the Plan is in material compliance with all applicable state, foreign and other securities and other laws applicable to the Plan. If on a Purchase Date in any Offering hereunder the Plan is not so registered or in such compliance, no rights granted under the Plan or any Offering shall be exercised on such Purchase Date, and the Purchase Date shall be delayed until the Plan is subject to such an effective registration statement and such compliance, except that the Purchase Date shall not be delayed more than twelve (12) months and the Purchase Date shall in no event be more than twenty-seven (27) months from the Offering Date. If on the Purchase Date of any Offering hereunder, as delayed to the maximum extent permissible, the Plan is not registered and in such compliance, no rights granted under the Plan or any Offering shall be exercised and all payroll deductions accumulated during the Offering (reduced to the extent, if any, such deductions have been used to acquire stock) shall be distributed to the participants, without interest.

9. COVENANTS OF THE COMPANY.

(a) During the terms of the rights granted under the Plan, the Company shall keep available at all times the number of shares of stock required to satisfy such rights.

(b) The Company shall seek to obtain from each federal, state, foreign or other regulatory commission or agency having jurisdiction over the Plan such authority as may be required to issue and sell shares of stock upon exercise of the rights granted under the Plan. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority which counsel for the Company deems necessary for the lawful issuance and sale of stock under the Plan, the Company shall be relieved from any liability for failure to issue and sell stock upon exercise of such rights unless and until such authority is obtained.

10. USE OF PROCEEDS FROM STOCK.

Proceeds from the sale of stock pursuant to rights granted under the Plan shall constitute general funds of the Company.

11. RIGHTS AS A STOCKHOLDER.

A participant shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares subject to rights granted under the Plan unless and until the participant's shareholdings acquired upon exercise of rights under the Plan are recorded in the books of the Company.

12. ADJUSTMENTS UPON CHANGES IN STOCK.

(a) If any change is made in the stock subject to the Plan, or subject to any rights granted under the Plan, due to a change in corporate capitalization and without the receipt of consideration by the Company (through reincorporation, stock dividend, stock split, reverse stock split, combination or reclassification of shares), the Plan will be appropriately adjusted in the class(es) and maximum number of securities subject to the Plan pursuant to subsection 3(a), and the outstanding rights will be appropriately adjusted in the class(es) and number of securities and price per share of stock subject to such outstanding rights. Such adjustments shall be made by the Board, the determination of which shall be final, binding and conclusive.

(b) In the event of: (1) a dissolution, liquidation or sale of all or substantially all of the securities or assets of the Company, (2) a merger or consolidation in which the Company is not the surviving corporation or (3) a reverse merger in which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise, then any surviving corporation may assume outstanding rights or substitute similar rights for those under the Plan. In the event that no surviving corporation assumes outstanding rights or substitutes similar rights therefor, participants' accumulated payroll deductions shall be used to purchase Common Stock immediately prior to the transaction described above and the

participants' rights under the ongoing Offering shall terminate immediately following such purchase.

13. AMENDMENT OF THE PLAN.

(a) The Board at any time, and from time to time, may amend the Plan. However, except as provided in paragraph 12 relating to adjustments upon changes in stock, no amendment shall be effective unless approved by the stockholders of the Company within twelve (12) months before or after the adoption of the amendment, where the amendment will:

(i) Increase the number of shares reserved for rights under the Plan;

(ii) Modify the provisions as to eligibility for participation in the Plan (to the extent such modification requires stockholder approval in order for the Plan to obtain employee stock purchase plan treatment under Section 423 of the Code or to comply with the requirements of Rule 16b-3 promulgated under the Securities Exchange Act of 1934, as amended ("Rule 16b-3")); or

(iii) Modify the Plan in any other way if such modification requires stockholder approval in order for the Plan to obtain employee stock purchase plan treatment under Section 423 of the Code or to comply with the requirements of Rule 16b-3.

It is expressly contemplated that the Board may amend the Plan in any respect the Board deems necessary or advisable to provide eligible employees with the maximum benefits provided or to be provided under the provisions of the Code and the regulations promulgated thereunder relating to employee stock purchase plans and/or to bring the Plan and/or rights granted under it into compliance

therewith.

(b) Rights and obligations under any rights granted before amendment of the Plan shall not be impaired by any amendment of the Plan, except with the consent of the person to whom such rights were granted, or except as necessary to comply with any laws or governmental regulations, or except as necessary to ensure that the Plan and/or rights granted under the Plan comply with the requirements of Section 423 of the Code.

14. DESIGNATION OF BENEFICIARY.

(a) A participant may file a written designation of a beneficiary who is to receive any shares and cash, if any, from the participant's account under the Plan in the event of such participant's death subsequent to the end of an Offering but prior to delivery to the participant of such shares and cash. In addition, a participant may file a written designation of a beneficiary who is to receive any cash from the participant's account under the Plan in the event of such participant's death during an Offering.

(b) Such designation of beneficiary may be changed by the participant at any time by written notice. In the event of the death of a participant and in the absence of a beneficiary validly designated under the Plan who is living at the time of such participant's death, the

Company shall deliver such shares and/or cash to the executor or administrator of the estate of the participant, or if no such executor or administrator has been appointed (to the knowledge of the Company), the Company, in its sole discretion, may deliver such shares and/or cash to the spouse or to any one or more dependents or relatives of the participant, or if no spouse, dependent or relative is known to the Company, then to such other person as the Company may designate.

15. TERMINATION OR SUSPENSION OF THE PLAN.

(a) The Board in its discretion, may suspend or terminate the Plan at any time. No rights may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) Rights and obligations under any rights granted while the Plan is in effect shall not be altered or impaired by suspension or termination of the Plan, except as expressly provided in the Plan or with the consent of the person to whom such rights were granted, or except as necessary to comply with any laws or governmental regulation, or except as necessary to ensure that the Plan and/or rights granted under the Plan comply with the requirements of Section 423 of the Code.

(c) Notwithstanding the foregoing, the Plan shall terminate and no rights may be granted under the Plan after the tenth anniversary of the Effective Date.

16. EFFECTIVE DATE OF PLAN.

The Plan shall become effective simultaneously with the effectiveness of the Company's registration statement under the Securities Act with respect to the initial public offering of shares of the Company's Common Stock (the "Effective Date"), but no rights granted under the Plan shall be exercised unless and until the Plan has been approved by the stockholders of the Company within twelve (12) months before or after the date the Plan is adopted by the Board, which date may be prior to the Effective Date.

EXHIBIT 10.5

RIGEL PHARMACEUTICALS, INC.

2000 NON-EMPLOYEE DIRECTORS' STOCK OPTION PLAN

ADOPTED AUGUST 18, 2000
APPROVED BY STOCKHOLDERS _____, 2000
EFFECTIVE DATE: _____, 2000

1. PURPOSES.

(a) ELIGIBLE OPTION RECIPIENTS. The persons eligible to receive Options are the Non-Employee Directors of the Company.

(b) AVAILABLE OPTIONS. The purpose of the Plan is to provide a means by which Non-Employee Directors may be given an opportunity to benefit from increases in value of the Common Stock through the granting of Nonstatutory Stock Options.

(c) GENERAL PURPOSE. The Company, by means of the Plan, seeks to retain the services of its Non-Employee Directors, to secure and retain the services of new Non-Employee Directors and to provide incentives for such persons to exert maximum efforts for the success of the Company and its Affiliates.

2. DEFINITIONS.

(a) "AFFILIATE" means any parent corporation or subsidiary corporation of the Company, whether now or hereafter existing, as those terms are defined in Sections 424(e) and (f), respectively, of the Code.

(b) "ANNUAL GRANT" means an Option granted annually to all Non-Employee Directors who meet the criteria specified in subsection 6(b) of the Plan.

(c) "ANNUAL MEETING" means the annual meeting of the stockholders of the Company.

(d) "BOARD" means the Board of Directors of the Company.

(e) "CODE" means the Internal Revenue Code of 1986, as amended.

(f) "COMMON STOCK" means the common stock of the Company.

(g) "COMPANY" means Rigel Pharmaceuticals, Inc., a Delaware corporation.

(h) "CONSULTANT" means any person, including an advisor, (i) engaged by the Company or an Affiliate to render consulting or advisory services and who is compensated for such services or (ii) who is a member of the Board of Directors of an Affiliate. However, the term "Consultant" shall not include either Directors of the Company who are not compensated

by the Company for their services as Directors or Directors of the Company who are merely paid a director's fee by the Company for their services as Directors.

(i) "CONTINUOUS SERVICE" means that the Optionholder's service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. The Optionholder's Continuous Service shall not be deemed to have terminated merely because of a change in the capacity in which the Optionholder renders service to the Company or an Affiliate as an Employee, Consultant or Director or a change in the entity for which the Optionholder renders such service, provided that there is no interruption or termination of the Optionholder's service. For example, a change in status without interruption from a Non-Employee Director of the Company to a Consultant of an Affiliate or an Employee of the Company will not constitute an interruption of Continuous Service. The Board or the chief executive officer of the Company, in that party's sole discretion, may determine whether Continuous Service shall be considered interrupted in the case of any leave of absence approved by that party, including sick leave, military leave or any other personal leave.

(j) "DIRECTOR" means a member of the Board of Directors of the Company.

(k) "DISABILITY" means the permanent and total disability of a person within the meaning of Section 22(e)(3) of the Code.

(l) "EMPLOYEE" means any person employed by the Company or an Affiliate. Mere service as a Director or payment of a director's fee by the Company or an Affiliate shall not be sufficient to constitute "employment" by the Company or an Affiliate.

(m) "EXCHANGE ACT" means the Securities Exchange Act of 1934, as amended.

(n) "FAIR MARKET VALUE" means, as of any date, the value of the Common Stock determined as follows:

(i) If the Common Stock is listed on any established stock exchange or traded on the Nasdaq National Market or the Nasdaq SmallCap Market, the Fair Market Value of a share of Common Stock shall be the closing sales price for such stock (or the closing bid, if no sales were reported) as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Common Stock) on the last market trading day prior to the day of determination, as reported in The Wall Street Journal or such other source as the Board deems reliable.

(ii) In the absence of such markets for the Common Stock, the Fair Market Value shall be determined in good faith by the Board.

(o) "INITIAL GRANT" means an Option granted to a Non-Employee Director who meets the criteria specified in subsection 6(a) of the Plan.

(p) "IPO DATE" means the effective date of the initial public offering of the Common Stock.

(q) "NON-EMPLOYEE DIRECTOR" means a Director who is not an Employee.

(r) "NONSTATUTORY STOCK OPTION" means an Option not intended to qualify as an incentive stock option within the meaning of Section 422 of the Code and the regulations promulgated thereunder.

(s) "OFFICER" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act and the rules and regulations promulgated thereunder.

(t) "OPTION" means a Nonstatutory Stock Option granted pursuant to the Plan.

(u) "OPTION AGREEMENT" means a written agreement between the Company and an Optionholder evidencing the terms and conditions of an individual Option grant. Each Option Agreement shall be subject to the terms and conditions of the Plan.

(v) "OPTIONHOLDER" means a person to whom an Option is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Option.

(w) "PLAN" means this Rigel Pharmaceuticals, Inc. 2000 Non-Employee Directors' Stock Option Plan.

(x) "RULE 16b-3" means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.

(y) "SECURITIES ACT" means the Securities Act of 1933, as amended.

3. ADMINISTRATION.

(a) ADMINISTRATION BY BOARD. The Board shall administer the Plan. The Board may not delegate administration of the Plan to a committee.

(b) POWERS OF BOARD. The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine the provisions of each Option to the extent not specified in the Plan.

(ii) To construe and interpret the Plan and Options granted under it, and to establish, amend and revoke rules and regulations for its administration. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Option Agreement, in a manner and to the extent it shall deem necessary or expedient to make the Plan fully effective.

(iii) To amend the Plan or an Option as provided in Section 12.

(iv) To terminate or suspend the Plan as provided in Section 13.

(v) Generally, to exercise such powers and to perform such

acts as the Board deems necessary or expedient to promote the best interests of the Company that are not in conflict with the provisions of the Plan.

(c) EFFECT OF BOARD'S DECISION. All determinations, interpretations and constructions made by the Board in good faith shall not be subject to review by any person and shall be final, binding and conclusive on all persons.

4. SHARES SUBJECT TO THE PLAN.

(a) SHARE RESERVE. Subject to the provisions of Section 11 relating to adjustments upon changes in the Common Stock, the Common Stock that may be issued pursuant to Options shall not exceed in the aggregate three hundred thousand (300,000) shares of Common Stock.

(b) REVERSION OF SHARES TO THE SHARE RESERVE. If any Option shall for any reason expire or otherwise terminate, in whole or in part, without having been exercised in full, the shares of Common Stock not acquired under such Option shall revert to and again become available for issuance under the Plan.

(c) SOURCE OF SHARES. The shares of Common Stock subject to the Plan may be unissued shares or reacquired shares, bought on the market or otherwise.

5. ELIGIBILITY.

The Options as set forth in section 6 automatically shall be granted under the Plan to all Non-Employee Directors.

6. NON-DISCRETIONARY GRANTS.

(a) INITIAL GRANTS. Without any further action of the Board, each person who is elected or appointed for the first time to be a Non-Employee Director after the IPO Date automatically shall, upon the date of his or her initial election or appointment to be a Non-Employee Director by the Board or stockholders of the Company, be granted an Initial Grant to purchase twenty thousand (20,000) shares of Common Stock on the terms and conditions set forth herein.

(b) ANNUAL GRANTS. Without any further action of the Board, a Non-Employee Director shall be granted an Annual Grant as follows: On the day following each Annual Meeting commencing with the Annual Meeting in 2001, each person who is then a Non-Employee Director automatically shall be granted an Annual Grant to purchase five thousand (5,000) shares of Common Stock on the terms and conditions set forth herein; PROVIDED, HOWEVER, that if the person has not been serving as a Non-Employee Director for the entire period since the preceding Annual Meeting, then the number of shares subject to the Annual Grant shall be reduced pro rata for each full quarter prior to the date of grant during which such person did not serve as a Non-Employee Director.

7. OPTION PROVISIONS.

Each Option shall be in such form and shall contain such terms and conditions as required by the Plan. Each Option shall contain such additional terms and conditions, not inconsistent with the Plan, as the Board shall deem appropriate. Each Option shall include (through incorporation of provisions hereof by reference in the Option or otherwise) the substance of each of the following provisions:

(a) TERM. No Option shall be exercisable after the expiration of ten (10) years from the date it was granted.

(b) EXERCISE PRICE. The exercise price of each Option shall be one hundred percent (100%) of the Fair Market Value of the stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, an Option may be granted with an exercise price lower than that set forth in the preceding sentence if such Option is granted pursuant to an assumption or substitution for another option in a manner satisfying the provisions of Section 424(a) of the Code.

(c) CONSIDERATION. The purchase price of stock acquired pursuant to an Option may be paid, to the extent permitted by applicable statutes and regulations, in any combination of the following methods:

(i) By cash or check.

(ii) Provided that at the time of exercise the Common Stock is publicly traded and quoted regularly in THE WALL STREET JOURNAL, by delivery of already-owned shares of Common Stock either that the Optionholder has held for the period required to avoid a charge to the Company's reported earnings (generally six months) or that the Optionholder did not acquire, directly or indirectly from the Company, that are owned free and clear of any liens, claims, encumbrances or security interests, and that are valued at Fair Market Value on the date of exercise. "Delivery" for these purposes

shall include delivery to the Company of the Optionholder's attestation of ownership of such shares of Common Stock in a form approved by the Company. Notwithstanding the foregoing, the Optionholder may not exercise the Option by tender to the Company of Common Stock to the extent such tender would violate the provisions of any law, regulation or agreement restricting the redemption of the Company's stock.

(iii) Provided that at the time of exercise the Common Stock is publicly traded and quoted regularly in THE WALL STREET JOURNAL, pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board that, prior to the issuance of Common Stock, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds.

(d) TRANSFERABILITY. An Option is transferable by will or by the laws of descent and distribution. An Option also is transferable (i) by instrument to an inter vivos or testamentary trust, in a form accepted by the Company, in which the Option is to be passed to beneficiaries

upon the death of the trustor (settlor) and (ii) by gift, in a form accepted by the Company, to a member of the "immediate family" of the Optionholder as that term is defined in 17 C.F.R. 240.16a-1(e). An Option shall be exercisable during the lifetime of the Optionholder only by the Optionholder and a permitted transferee as provided herein. However, the Optionholder may, by delivering written notice to the Company, in a form satisfactory to the Company, designate a third party who, in the event of the death of the Optionholder, shall thereafter be entitled to exercise the Option.

(e) EXERCISE SCHEDULE. The Option shall be exercisable as the shares of Common Stock subject to the Option vest.

(f) VESTING SCHEDULE. Options shall vest as follows:

(i) Initial Grants shall provide for vesting of eight hundred thirty-four (834) of the shares of Common Stock subject to the Option each month after the date of grant.

(ii) Annual Grants shall provide for vesting of two hundred nine (209) of the shares of Common Stock subject to the Option each month after the date of the grant.

(g) TERMINATION OF CONTINUOUS SERVICE. In the event an Optionholder's Continuous Service terminates (other than upon the Optionholder's death or Disability), the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise it as of the date of termination) but only within such period of time ending on the earlier of (i) the date three (3) months following the termination of the Optionholder's Continuous Service, or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination, the Optionholder does not exercise his or her Option within the time specified in the Option Agreement, the Option shall terminate.

(h) EXTENSION OF TERMINATION DATE. If the exercise of the Option following the termination of the Optionholder's Continuous Service (other than upon the Optionholder's death or Disability) would be prohibited at any time solely because the issuance of shares would violate the registration requirements under the Securities Act, then the Option shall terminate on the earlier of (i) the expiration of the term of the Option set forth in subsection 7(a) or (ii) the expiration of a period of three (3) months after the termination of the Optionholder's Continuous Service during which the exercise of the Option would not be in violation of such registration requirements.

(i) DISABILITY OF OPTIONHOLDER. In the event an Optionholder's Continuous Service terminates as a result of the Optionholder's Disability, the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise it as of the date of termination), but only within such period of time ending on the earlier of (i) the date twelve (12) months following such termination or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination, the Optionholder does not exercise his or her Option within the time specified herein, the Option shall terminate.

(j) DEATH OF OPTIONHOLDER. In the event (i) an Optionholder's Continuous Service terminates as a result of the Optionholder's death or (ii) the Optionholder dies within the three-month period after the termination of the Optionholder's Continuous Service for a reason other than death, then the Option may be exercised (to the extent the Optionholder was entitled to exercise the Option as of the date of death) by the Optionholder's estate, by a person who acquired the right to exercise the Option by bequest or inheritance or by a

person designated to exercise the Option upon the Optionholder's death, but only within the period ending on the earlier of (1) the date eighteen (18) months following the date of death or (2) the expiration of the term of such Option as set forth in the Option Agreement. If, after death, the Option is not exercised within the time specified herein, the Option shall terminate.

8. COVENANTS OF THE COMPANY.

(a) AVAILABILITY OF SHARES. During the terms of the Options, the Company shall keep available at all times the number of shares of Common Stock required to satisfy such Options.

(b) SECURITIES LAW COMPLIANCE. The Company shall seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Options and to issue and sell shares of Common Stock upon exercise of the Options; provided, however, that this undertaking shall not require the Company to register under the Securities Act the Plan, any Option or any stock issued or issuable pursuant to any such Option. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority which counsel for the Company deems necessary for the lawful issuance and sale of stock under the Plan, the Company shall be relieved from any liability for failure to issue and sell stock upon exercise of such Options unless and until such authority is obtained.

9. USE OF PROCEEDS FROM STOCK.

Proceeds from the sale of stock pursuant to Options shall constitute general funds of the Company.

10. MISCELLANEOUS.

(a) STOCKHOLDER RIGHTS. No Optionholder shall be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares subject to such Option unless and until such Optionholder has satisfied all requirements for exercise of the Option pursuant to its terms.

(b) NO SERVICE RIGHTS. Nothing in the Plan or any instrument executed or Option granted pursuant thereto shall confer upon any Optionholder any right to continue to serve the Company as a Non-Employee Director or shall affect the right of the Company or an Affiliate to terminate (i) the employment of an Employee with or without notice and with or without cause, (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or an Affiliate or (iii) the service of a Director pursuant to the Bylaws of the Company

or an Affiliate, and any applicable provisions of the corporate law of the state in which the Company or the Affiliate is incorporated, as the case may be.

(c) INVESTMENT ASSURANCES. The Company may require an Optionholder, as a condition of exercising or acquiring stock under any Option, (i) to give written assurances satisfactory to the Company as to the Optionholder's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Option; and (ii) to give written assurances satisfactory to the Company stating that the Optionholder is acquiring the stock subject to the Option for the Optionholder's own account and not with any present intention of selling or otherwise distributing the stock. The foregoing requirements, and any assurances given pursuant to such requirements, shall be inoperative if (iii) the issuance of the shares upon the exercise or acquisition of stock under the Option has been registered under a then currently effective registration statement under the Securities Act or (iv) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on stock certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the stock.

(d) WITHHOLDING OBLIGATIONS. The Optionholder may satisfy any federal, state or local tax withholding obligation relating to the exercise or acquisition of stock under an Option by any of the following means (in addition to the Company's right to withhold from any compensation paid to the Optionholder by the Company) or by a combination of such means: (i) tendering a cash payment; (ii) authorizing the Company to withhold shares from the shares of the Common Stock otherwise issuable to the Optionholder as a result of the exercise or acquisition of stock under the Option, provided, however, that no shares of Common Stock are withheld with a value exceeding the minimum amount of tax required to be withheld by law; or (iii) delivering to the Company owned and unencumbered shares of the Common Stock.

11. ADJUSTMENTS UPON CHANGES IN STOCK.

(a) CAPITALIZATION ADJUSTMENTS. If any change is made in the stock subject to the Plan, or subject to any Option, without the receipt of consideration by the Company (through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other transaction not involving the receipt of consideration by the Company), the Plan will be appropriately adjusted in the class(es) and maximum number of securities subject both to the Plan pursuant to subsection 4(a) and to the nondiscretionary Options specified in Section 5, and the outstanding Options will be appropriately adjusted in the class(es) and number of securities and price per share of stock subject to such outstanding Options. The Board shall make such adjustments, and its determination shall be final, binding and conclusive. (The conversion of any convertible

securities of the Company shall not be treated as a transaction "without receipt of consideration" by the Company.)

(b) DISSOLUTION OR LIQUIDATION. In the event of a dissolution or liquidation of the Company, then all outstanding Options shall terminate immediately prior to such event.

(c) CHANGE IN CONTROL. In the event of (i) a sale, lease or other disposition of all or substantially all of the securities or assets of the Company, (ii) a merger or consolidation in which the Company is not the surviving corporation or (iii) a reverse merger in which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise, then any surviving corporation or acquiring corporation may assume any Options outstanding under the Plan or may substitute similar Options (including an option to acquire the same consideration paid to the stockholders in the transaction described in this subsection 11(c)) for those outstanding under the Plan. In the event no surviving corporation or acquiring corporation assumes such Options or substitutes similar Options for those outstanding under the Plan, then with respect to Options held by Optionholders whose Continuous Service has not terminated, the vesting of such Options (and the time during which such Options may be exercised) shall be accelerated in full, and the Options shall terminate if not exercised at or prior to such event. With respect to any other Options outstanding under the Plan, such Options shall terminate if not exercised prior to such event.

12. AMENDMENT OF THE PLAN AND OPTIONS.

(a) AMENDMENT OF PLAN. The Board at any time, and from time to time, may amend the Plan. However, except as provided in Section 11 relating to adjustments upon changes in stock, no amendment shall be effective unless approved by the stockholders of the Company to the extent stockholder approval is necessary to satisfy the requirements of Rule 16b-3 or any Nasdaq or securities exchange listing requirements.

(b) STOCKHOLDER APPROVAL. The Board may, in its sole discretion, submit any other amendment to the Plan for stockholder approval.

(c) NO IMPAIRMENT OF RIGHTS. Rights under any Option granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (i) the Company requests the consent of the Optionholder and (ii) the Optionholder consents in writing.

(d) AMENDMENT OF OPTIONS. The Board at any time, and from time to time, may amend the terms of any one or more Options; provided, however, that the rights under any Option shall not be impaired by any such amendment unless (i) the Company requests the consent of the Optionholder and (ii) the Optionholder consents in writing.

13. TERMINATION OR SUSPENSION OF THE PLAN.

(a) PLAN TERM. The Board may suspend or terminate the Plan at any time. No Options may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) NO IMPAIRMENT OF RIGHTS. Suspension or termination of the Plan shall not impair rights and obligations under any Option granted while the Plan is in effect except with the written consent of the Optionholder.

14. EFFECTIVE DATE OF PLAN.

The Plan shall become effective on the IPO Date, but no Option shall be exercised unless and until the Plan has been approved by the stockholders of the Company, which approval shall be within twelve (12) months before or after the date the Plan is adopted by the Board.

15. CHOICE OF LAW.

All questions concerning the construction, validity and interpretation of this Plan shall be governed by the law of the State of Delaware, without regard to such state's conflict of laws rules.

EXHIBIT 10.6

COLLABORATION AGREEMENT

THIS COLLABORATION AGREEMENT (the "Agreement") is entered into as of December 4, 1998 (the "Effective Date") by and between RIGEL PHARMACEUTICALS, INC., a Delaware corporation ("Rigel") with its offices at 772 Lucerne Drive, Sunnyvale, California 94086, and JANSSEN PHARMACEUTICA N.V., a Belgian corporation ("Janssen") with offices at Turnhoutseweg 30, 2340 Beerse, Belgium (Rigel and Janssen individually referred to as "Party", and collectively as "Parties").

RECITALS

WHEREAS, Rigel is a leader in the discovery and validation of functional peptide-target interactions regulating the cell cycle in specific tumor cells; and

WHEREAS, Janssen is engaged in the research, development, marketing, manufacture and distribution of pharmaceutical compounds useful in treating or preventing human diseases and conditions; and

WHEREAS, Rigel and Janssen desire to enter into a collaborative relationship to conduct research to identify novel targets for drug discovery, as generally described in the Research Plan, with Janssen developing and commercializing any compounds resulting therefrom; and

WHEREAS, Rigel and Janssen agree that they will conduct the research under this Agreement on a collaborative basis with a goal of discovering and identifying products that are suitable for commercialization; and

WHEREAS, Johnson & Johnson Development Corporation has agreed to purchase and Rigel has agreed to sell one million five hundred thousand (1,500,000) shares of Rigel Series D Preferred Stock with a total value of US$3 million pursuant to a stock purchase agreement between the Parties of even date herewith (the "Stock Purchase Agreement"); and

WHEREAS, if the research collaboration is successful, the resulting compounds may have a broad range of applications, particularly in the diagnosis, therapeutic treatment and/or prevention of certain tumors and other diseases;

NOW, THEREFORE, in consideration of the foregoing and the covenants and promises contained in this Agreement, the Parties agree as follows:

1. DEFINITIONS

As used herein, the following terms shall have the following meanings:

1.1 "ACTIVE PEPTIDE" shall mean a molecule which changes cellular function in an assay specified by the RMC.

1.2 "AFFILIATE" shall mean any company or entity controlled by, controlling, or under common control with a Party hereto and shall include without limitation any company fifty percent (50%) or more of whose voting stock or participating profit interest is owned or controlled, directly or indirectly, by a Party, and any company which owns or controls, directly or indirectly, fifty percent (50%) or more of the voting stock of a Party.

1.3 "CONFIDENTIAL INFORMATION" shall mean all information (generally not known to the public), inventions, know-how or data disclosed by a Party to the other pursuant to this Agreement including, without limitation, Rigel Know-How, Janssen Know-How, manufacturing, marketing, financial, personnel, scientific and other business information and plans, and the material terms of this Agreement, whether in oral, written, graphic or electronic form.

1.4 "CONTROL" shall mean the possession of the ability to grant a license or sublicense to know-how and patents without violating the terms of any agreement or other arrangement with, or the rights of, any Third Party.

1.5 "DATE OF FIRST SALE" means the day on which Janssen, its Affiliate or its sublicensee first sells a Product to a Third Party in an arm's length transaction.

1.6 "DEVELOPMENT CANDIDATE" shall mean a compound selected for pre-phase I studies, including, but not limited to, GLP toxicological and pharmacological studies using GMP material.

1.7 "DIAGNOSTIC PRODUCT" shall mean any composition of matter used for the diagnosis of a disease or condition, including but not limited to, the diagnosis of disease susceptibility, or a choice of treatment or monitoring of a disease or condition, or the determination of genetic traits where such composition of matter is a component of a Validated Target-Peptide Pair or was identified by or on behalf of Rigel or Janssen in a Janssen Collaboration Assay and/or a Janssen Non-Collaboration Assay.

1.8 "EXCLUSIVITY TERM" shall have the meaning assigned to it in Section 3.6.

1.9 "FDA" means the United States Food and Drug Administration.

1.10 "FIELD OF RESEARCH" shall mean the identification of Molecular Targets and the related Active Peptides which cause alterations in the cell cycle of human tumor cells, including changes in the capacity to transit through various cell cycle stages, and restoration of normal cell cycle progression which would result in the inhibition of proliferation or the induction of apoptosis in these human tumor cells.

1.11 "FTE" shall mean the equivalent of a full-time scientist based on at least of 47 (forty-seven) weeks per year of scientific work carried out by one or more employees or consultants of Rigel, each of whom devotes a portion of his or her time to scientific work on or directly related to the Research Program; PROVIDED, HOWEVER, that Janssen understands and agrees that Rigel retains complete discretion to change the identity, the frequency and time which any individual employee devotes to the Research Program. Scientific work on or directly related to the Research Program to be performed by Rigel employees or consultants can include, but is not limited to, experimental laboratory work, recording and writing up results, reviewing literature and references, attending selected and appropriate seminars and symposia, managing and leading scientific staff, and carrying out Research Program management duties (including service on the Research Management Committee).

1.12 "HOMOLOGUE" shall mean a modification to one of the components of a VTPP which is functionally equivalent to such VTPP component.

1.13 "INTERNAL JANSSEN RESEARCH" shall mean the internal research conducted by Janssen and its permitted sublicensees using Rigel Technology or with Rigel Technology Assays, to assess the alteration or normalization of uncontrolled cell growth, cell division, dissemination or differentiation status of cancer cells.

1.14 "JANSSEN COLLABORATION ASSAY" shall mean a drug discovery assay incorporating a Janssen Collaboration Target.

1.15 "Janssen Know-How" shall mean any and all tangible or intangible know-how, trade secrets, inventions (whether or not patentable), data, preclinical and clinical results, physical, chemical or biological material, and other information that is necessary and useful in the Field of Research and that Janssen owns or Controls on the Effective Date and any replication or any part of such information or material. Janssen Know-How shall exclude Janssen Patents.

1.16 "JANSSEN PATENTS" shall mean all foreign and domestic patents (including, without limitation, extensions, reissues, reexaminations, renewals and inventors certificates) issued as of, and patents issuing from patent applications (including substitutions, provisionals, divisionals, continuations and continuations-in-part) that are pending as of, the Effective Date which claim inventions or discoveries necessary and useful in the Field of Research and are owned or Controlled by Janssen. The RMC shall compile a list of Janssen Patents from time to time.

1.17 "JANSSEN COLLABORATION TARGET" means a Validated Target-Peptide Pair delivered by Rigel as provided in Section 3.5.

1.18 "JANSSEN TECHNOLOGY" shall mean Janssen Patents and Janssen Know-How.

1.19 "MAJOR MARKET" shall mean the U.S.A., France, Germany, United Kingdom or any country in the EU pursuant to an NDA approval by the EMEA, or Japan.

1.20 "MOLECULAR TARGET" shall mean a molecule shown in an assay specified by the RMC to play a role in a research pathway in human tumor cells.

1.21 "NDA" shall mean a New Drug Application or its equivalent for biological products as more fully defined in 21 C.F.R. Section 314.5 et seq., and any equivalent filing in any regulatory jurisdiction.

1.22 "NET SALES" means the gross sales price billed by Janssen or an Affiliate thereof or a sub-licensee thereof for sales of Products hereunder to a Third Party less (in each case as may be applicable thereto and consistent with such Party's then existing standard business practices): (a) standard trade discounts, including cash discounts or rebates, actually allowed or granted from the billed amount, (b) credits or allowances actually granted upon claims, rejections or returns of Products, including recalls, regardless of the party requesting such recall, (c) charges included as part of the gross sales price for freight, postage, shipping and insurance charges, to the extent specifically billed, (d) taxes (other than income taxes), duties or other governmental charges levied on or measured by the billing amount when included in billing, as adjusted for rebates and refunds, and (e) accounts that are uncollectible and written off Janssen's books as uncollectible, provided that any uncollectible accounts excluded pursuant to this clause (e) which are subsequently collected by Janssen shall be included in Net Sales for the royalty period in which such amounts are collected. In the event any Product is sold in the form of a combination containing one or more active ingredients in addition to a Product, Net Sales for such combination will be calculated by multiplying actual Net Sales of such combination by the fraction A/(A+B), where A is the invoice price of the applicable Product, if sold separately, and B is the total invoice price of any other active component or components, or non-consumable devices (such as, for example, implantable pumps or electronic stimulators; however, items such as, for example, disposable transdermal patches or prefilled syringes shall constitute consumable devices) in the combination, if sold separately. If, on a country-by-country basis, the other active component or components in the combination are not sold separately in said country, Net Sales for the purpose of determining royalties of the combination shall be calculated by multiplying actual Net Sales of such combination by the fraction A/C, where A is the invoice price of the applicable Product, if sold separately, and C is the invoice price of the combination. If, on a country-by-country basis, neither the Product nor the other active component or components of the combination is sold separately in said country, Net Sales for the purposes of determining royalties of the combination shall be determined by the Parties in good faith.

1.23 "NON-COLLABORATION PHARMACEUTICAL PRODUCT" shall mean a composition of matter, including, but not limited to a chemical entity, a pro-drug, an isomer, a non-peptide, and a protein or nucleic acid or any fragment thereof, that was identified by or on behalf of Janssen or its permitted sublicensees in the Internal Janssen Research, that is useful for treating and/or preventing human diseases.

1.24 "PHARMACEUTICAL COLLABORATION PRODUCT" shall mean a composition of matter, including, but not limited to, a chemical entity, a pro drug, an isomer, a non-peptide, and a protein or nucleic acid or any fragment thereof, that was identified by or on behalf of Rigel or Janssen in a Janssen Collaboration Assay, that is useful for treating and/or preventing human

diseases; PROVIDED, HOWEVER, that the term "Pharmaceutical Collaboration Product" specifically excludes any composition of matter marketed or being developed by Janssen as of the Effective Date.

1.25 "PHASE III CLINICAL TRIAL" shall mean that clinical trial of a Product designed to be on a sufficient number of patients to establish the safety and efficacy of a Product and generate pharmacoeconomic data to support regulatory approval in a therapeutic indication as more fully defined in 21 C.F.R. 312.21(c), or any equivalent clinical trial in a non-U.S. regulatory jurisdiction.

1.26 "PRELIMINARY TARGET-PEPTIDE PAIRS" shall mean a Molecular Target together with an Active Peptide that binds thereto, which pair has been identified or discovered in the course of the Research Program, and which has been Validated Preliminarily.

1.27 "PRODUCTS" shall mean the Pharmaceutical Collaboration Products, the Target-Peptide Therapeutic Products, the Diagnostic Products and the Non-Collaboration Pharmaceutical Products.

1.28 "REGULATORY APPROVAL" shall mean any approval (including price and reimbursement approvals), licenses, registrations, or authorizations of any federal, state or local regulatory agency, department, bureau or other government entity, necessary for the manufacture, use, storage, import,

transport or sale of a Product in a regulatory jurisdiction.

1.29 "RESEARCH MANAGEMENT COMMITTEE" OR "RMC" shall mean the committee formed pursuant to Section 2.1.

1.30 "RESEARCH PERIOD" shall have the meaning assigned to it in Section 3.3.

1.31 "RESEARCH PLAN" shall mean the research plan attached as Exhibit A to this Agreement, as it may be modified or amended from time to time as permitted herein.

1.32 "RESEARCH PROGRAM" shall mean the program of the collaborative research as described in Article 3.

1.33 "RESEARCH PROGRAM KNOW-HOW" shall mean any tangible or intangible know-how, trade secrets, inventions (whether or not patentable), data, preclinical and clinical results, physical, chemical or biological material, and other information, including information concerning target-peptide interaction developed in the Research Program (including, without limitation, the functional role of the Molecular Target involved) that is within the Field of Research, and any replication or any part of such information or material; PROVIDED, HOWEVER, that the term "Research Program Know-How" as defined specifically excludes Research Program Patents and any compounds identified in Internal Janssen Research.

1.34 "RESEARCH PROGRAM PATENTS" shall mean all foreign and domestic patents (including extensions, reissues, reexaminations, renewals and inventors certificates) issuing from applications (including substitutions, provisionals, divisionals, continuations and continuations-

in-part) that claim inventions that are made in the Research Program and that are filed by or on behalf of one or both of the Parties hereto.

1.35 "RESEARCH PROGRAM TECHNOLOGY" shall mean the Research Program Patents and Research Program Know-How.

1.36 "RIGEL TECHNOLOGY ASSAYS" shall mean the assays transferred to Janssen or its permitted sublicensees for use in the Internal Janssen Research which assess the alteration or normalization of uncontrolled cell growth, cell division, dissemination or differentiation status of cancer cells, which are more specifically listed in Exhibit B.

1.37 "RIGEL KNOW-HOW" shall mean any and all tangible or intangible know-how, trade secrets, inventions (whether or not patentable), data, preclinical and clinical results, physical, chemical or biological material, and other information that is necessary and useful in the Field of Research and that Rigel owns or Controls on the Effective Date and any replication or any part of such information or material, but subject to any limitations contained in any license agreements.

1.38 "RIGEL PATENTS" shall mean all foreign and domestic patents (including, without limitation, extensions, reissues, reexaminations, renewals and inventors certificates) issued as of, and patents issuing from applications (including substitutions, provisionals, divisionals, continuations and continuations-in-part) pending as of, the Effective Date which claim inventions or discoveries necessary and useful in the Field of Research and are owned or Controlled by Rigel, but subject to any limitations contained in any license agreements.

1.39 "RIGEL TECHNOLOGY" shall mean the Rigel Patents and Rigel Know-How.

1.40 "STANFORD AGREEMENTS" shall mean the agreements by and between Rigel and The Board of Trustees of Leland Stanford Junior University dated October 7, 1996 (the "1996 Agreement"), August 18, 1997 (the "1997 Agreement"), and March 27, 1998 (the "1998 Agreement"), which have been provided to Janssen with commercial terms redacted, and attached hereto as Exhibit D.

1.41 "STANFORD REQUIRED PROVISIONS" shall mean the provisions relating to (a) royalty reports, payments and accounting, (b) warranties or negation thereof, and (c) indemnity, contained respectively in Articles 8, 9 and 10 of the 1996 Agreement, Articles 7, 9 and 10 of the 1997 Agreement, and Articles 7, 8, and 9 of the 1998 Agreement.

1.42 "TARGET-PEPTIDE THERAPEUTIC PRODUCT" shall mean a product that contains a component of a VTPP or a Homologue thereof.

1.43 "TERM OF THE AGREEMENT" shall have the meaning assigned to it in Article 10.

1.44 "TERRITORY" shall mean the entire world.

1.45 "THIRD PARTY" shall mean any person or entity other than Janssen, Rigel and Affiliates of either.

1.46 "VALIDATED PRELIMINARILY" shall mean demonstration of a functional phenotype change in a primary assay and such other criteria as determined by the RMC prior to the commencement of target evaluation by Rigel.

1.47 "VALIDATED TARGET-PEPTIDE PAIR" OR "VTPP" shall mean a Molecular Target together with an Active Peptide that binds thereto, which pair has been identified or discovered during the course of the Research Program in the Field of Research, that meets the criteria for full validation established by the RMC at the time that the respective Preliminary Target Peptide Pair is selected for further validation.

2. RESEARCH PROGRAM GOVERNANCE

2.1 FORMATION OF RESEARCH MANAGEMENT COMMITTEE. The Research Program established by this Agreement shall be overseen by a Research Management Committee composed of an equal number of representatives from each Party (the "Research Management Committee") drawn from the ranks of senior scientists and senior research management of each Party. The total number of RMC members shall be agreed upon by the RMC from time to time. The Parties shall designate their representatives on the RMC within ten (10) days after the Effective Date. The Parties shall notify one another in writing of any change in the membership of the RMC as appropriate to allow for the participation of different research groups within Janssen and Rigel. The Parties shall agree upon the appropriate qualifications for members of the RMC and mechanisms for making substitutions for RMC members. An alternate member designated by a Party may serve temporarily in the absence of a permanent member of the RMC for such Party. Each Party shall designate one of its representatives as a co-chair of the RMC. Each co-chair of the RMC will be responsible for the agenda and the minutes of alternating RMC meetings.

2.2 RESEARCH PLAN DEVELOPMENT AND MODIFICATION. The RMC shall develop and periodically modify the Research Plan, commencing with the initial Research Plan attached hereto as Exhibit A.

2.3 RMC ACTIONS. In taking actions by the RMC, each Party shall have one vote. If the RMC fails to reach unanimity on a matter before it for decision, the matter shall be referred for resolution to the CEO of Rigel and the V.P. of Biological Research of Janssen for their consideration and agreement. If they are unable to agree after negotiation in good faith, the matter shall be resolved consistent with Janssen's position; PROVIDED, HOWEVER, that solely in connection with technical issues involving Rigel Technology such as, for example, how to carry out a certain experiment or which technique to be applied to obtain a certain result, such issues shall be resolved consistent with Rigel's position. Strategic decisions such as, for example, selection of Preliminary Target Peptide Pairs for further validation and the criteria for such validation, shall be resolved consistent with Janssen's position.

2.4 MEETINGS OF THE RMC. The RMC:

(a) shall hold meetings at such times and places as shall be determined by the RMC (it being expected that meetings will alternate between the U.S. and European offices of each party) but in no event shall such meetings be held in person less frequently than once every three (3) months during the first two (2) years after the Effective Date;

(b) may conduct meetings in person or by telephone conference, provided that meetings by telephone conference shall not reduce the number of meetings in person specified in paragraph (a) above;

(c) by mutual consent of the representatives of each Party, may invite other senior personnel of their organization to attend meetings of the RMC, as appropriate however such other senior personnel shall not have any duties of an RMC member.

(d) may act without a meeting if prior to such action a written

consent thereto is signed by all members of the RMC;

(e) may form and subsequently disband subcommittees with appropriate representation from each party; and

(f) may amend or expand upon the foregoing procedures for its internal operation by unanimous written consent.

2.5 MINUTES. At each meeting, the RMC shall elect a secretary who will prepare, within ten (10) days after each meeting (whether held in person or be telecommunication), the minutes reporting in reasonable detail the actions taken by the RMC, the status of the Research Program, issues requiring resolution and resolutions of previously reported issues, which minutes are to be signed by the RMC co-chair persons from each of the Parties.

2.6 SUBCOMMITTEES. Any subcommittee established by the RMC shall have appropriate representation of each Party and may include representatives who are not members of the RMC. Any such subcommittee shall be given assignments from the RMC, shall be subject to the authority of the RMC and shall report its actions to the RMC. At the request of either Party at any time, any such subcommittee shall be dissolved and its powers and functions returned to the RMC. The RMC shall not delegate any of its RMC Functions and Powers as described in Article 2.7, without retaining the final approval before implementing the subcommittee assignments.

2.7 RMC FUNCTIONS AND POWERS. The activities of the Parties under this Agreement shall be managed by the RMC only to the extent set forth herein (unless otherwise mutually agreed by the Parties). During the Research Period the RMC shall:

(a) determine the goals for the Research Program and establish and review the Research Plan for accomplishing such goals;

(b) encourage and facilitate ongoing cooperation and information exchange between the parties;

(c) monitor the progress of the Research Plan and the parties' diligence in carrying out their responsibilities thereunder;

(d) allocate tasks and coordinate activities required to perform the Research Plan;

(e) schedule routine visits by Rigel and Janssen personnel to Janssen and Rigel, respectively, and oversee secondment of Janssen and Rigel personnel pursuant to Section 3.9;

(f) establish prospective criteria to determine when a Molecular Target and Active Peptide is a Preliminary Target-Peptide Pair or a Validated Target-Peptide Pair, and to amend the Research Plan accordingly;

(g) identify and select Preliminary Target-Peptide Pairs and Validated Target-Peptide Pairs pursuant to Section 3.4 and 3.5;

(h) perform such other functions as expressly provided herein, as appropriate to further the purposes of this Agreement, as mutually agreed by the Parties.

2.8 OBLIGATIONS OF PARTIES DURING THE RESEARCH PERIOD. Janssen and Rigel shall provide the RMC with reasonable access during regular business hours to all Janssen Know-How, Rigel Know-How and Research Program Know-How specific to the Research Program that the RMC determines that is reasonably required in order to perform its obligations hereunder, subject to any bona fide obligations of confidentiality to a Third Party.

2.9 LIMITATIONS OF POWERS OF THE RMC. The RMC shall have no power to amend this Agreement and shall have only such powers as are specifically delegated to it hereunder.

3. CONDUCT OF RESEARCH PROGRAM

3.1 SCOPE OF THE RESEARCH PROGRAM. The Parties hereby agree to establish and conduct, during the Research Period, a collaborative research program pursuant to the Research Plan in the Field of Research, as described in this Article 3. The Parties will collaborate in producing Validated Target-Peptide Pairs in order to discover, develop and manufacture products useful in diagnosing, treating or preventing diseases in humans.

3.2 RESEARCH ACTIVITIES; REVISIONS.

(a) The Parties will perform research in the Field of Research as directed by the RMC and pursuant to the Research Plan. Modifications of the Research Plan shall be made in writing and only as directed and approved by the RMC. In the event of any such modification, Exhibit A, the obligations of the parties including, but not limited to, Rigel's resource obligations

under this Section 3.2 and Janssen's research support obligations under Section 6.2, shall be revised as necessary and appropriate, subject to written approval of the Parties.

(b) Rigel agrees to commit the resources set forth in this subsection (b), to exert the efforts necessary and reasonable and consistent with its normal business practices to execute and perform the Research Plan (including extensions for the balance of the Research Period), to maintain and utilize the scientific staff, laboratories, offices and other facilities consistent with such undertaking. Rigel and Janssen agree to reasonably cooperate with each other in the conduct of the Research Plan. The Parties hereby agree that Rigel's current laboratories; offices and other facilities are satisfactory for purposes of this Section 3.2. During the first three (3) years of the Research Period, Rigel shall commit 10 FTEs to the Research Program. The purchase of any item including, but not limited to, cell lines reasonably required by Rigel to conduct the Research Plan shall be Rigel's obligation and responsibility and all cost associated therewith shall be to Rigel's account.

3.3 RESEARCH PERIOD; EXTENSIONS. The Research Program will commence on the Effective Date and terminate three (3) years thereafter, unless extended by mutual agreement or unless this Agreement is terminated earlier as provided in Article 10 (the "Research Period"). Janssen shall have an option to extend the Research Period beyond the initial Research Period of three (3) years for additional one year periods for a total of two (2) years by giving notice to Rigel at least one hundred twenty (120) days prior to the anniversary of the end of the Research Period that it intends to exercise its option. The compensation per FTE will be at the payment level as set forth herein.

3.4 IDENTIFICATION OF PRELIMINARY TARGET-PEPTIDE PAIRS. During the Research Period, the RMC shall identify Preliminary Target-Peptide Pairs and shall issue a list thereof not less often than quarterly.

3.5 IDENTIFICATION OF VALIDATED TARGET-PEPTIDE PAIRS.

(a) During the Research Period, the RMC shall select Preliminary Target-Peptide Pairs to be further evaluated to determine whether they are suitable to be selected by the RMC as Validated Target-Peptide Pairs for the purpose of compound screening as provided in Section 3.6. Prior to commencing such evaluation, the RMC shall establish the criteria ("Validation Criteria") pursuant to Section 2.7(f) required for such Preliminary Target-Peptide Pairs to qualify as Validated Target-Peptide Pairs.

(b) Preliminary Target-Peptide Pairs for which it has not been established by the end of the Research Period whether or not they meet the Validation Criteria, shall revert to Rigel; PROVIDED, HOWEVER, that the Parties may determine that any Preliminary Target-Peptide Pair not fully validated may be transferred to Janssen for further validation as Internal Janssen Research.

(c) During the Research Period, the RMC shall issue a list of Validated Target-Peptide Pairs within thirty (30) days after each RMC meeting, and a final list thereof

within thirty (30) days after the end of the Research Period. Promptly after a Validated Target Peptide Pair has been listed, Rigel shall transfer all Research Program Technology necessary for Janssen to initiate screening with respect to that Validated Target Peptide Pair. Rigel shall not transfer any component of a Validated Target Peptide Pair to any Third Party without prior written approval of the Janssen.

3.6 COMPOUND SCREENING; DILIGENCE.

(a) Janssen may initiate compound screening with each Validated Target-Peptide Pair at any time during the first three (3) years following its determination by the RMC as a Validated Target-Peptide Pair (the "Exclusivity Term"). Janssen shall notify Rigel promptly upon the initiation of screening with each Validated Target-Peptide Pair.

(b) If Janssen does not initiate compound screening with a Validated Target-Peptide Pair during the Exclusivity Term pertaining to such

Validated Target-Peptide Pair, or, having timely initiated compound screening, Janssen fails to pursue such screening in a manner consistent with Janssen's normal research practices, then, in either case, the licenses granted herein by Rigel to Janssen for such Validated Target-Peptide Pair shall terminate and Janssen shall grant Rigel an exclusive, worldwide, royalty-free license, with the right to sublicense, under its interest in the Research Program Technology with respect to such Validated Target-Peptide Pair.

(c) If, according to Rigel, Janssen has failed to comply with the diligence requirements as set forth in subsection (b) above, Rigel shall notify Janssen thereof in writing. Within thirty (30) days of such notice, the Parties shall meet to discuss the matter. If no agreement is reached, the dispute shall be resolved as provided in Section 12.3. Effective upon such resolution, the licenses granted by Rigel hereunder shall terminate as provided in subsection (b) above, or shall continue, depending on whether or not Janssen is found to have breached the diligence obligations as described in subsection (b).

3.7 ADDITIONAL JANSSEN RIGHT TO VALIDATED TARGET-PEPTIDE PAIR. With respect to each Validated Target-Peptide Pair which reverts to Rigel as provided in Section 3.6, Rigel will, upon identifying a compound during the term of this Agreement which modulates the activity of such Validated Target-Peptide Pair or its constituents provide written notice to Janssen of such compound and provide the information reasonably necessary for Janssen to determine whether Janssen wishes to discuss licensing such compound. If Janssen notifies Rigel within ninety (90) days of Rigel's notice, of its desire to license such compound, the Parties will conduct good faith negotiations of terms upon which Rigel will license such compound to Janssen; PROVIDED, HOWEVER, if the Parties are unable to reach agreement within a further period of ninety (90) days (or such further period as the Parties may mutually agree) after Janssen's notice, then Janssen will have no rights with respect to such compound and Rigel will be free to exploit such compound alone or with others without obligation or liability to Janssen; PROVIDED, HOWEVER, that Rigel shall not enter into any agreement with a Third Party on terms which are substantially the same or less favorable to Rigel, than the terms last offered by Janssen.

3.8 RIGEL SCREENING. Rigel may initiate compound screening with a Validated Target-Peptide Pair upon the explicit written request of Janssen and acceptance by Rigel. However, Janssen shall have the exclusive right and license to develop and exploit any compound so identified or discovered by Rigel upon the terms provided in Sections 5.2 and 5.3.

3.9 SECONDMENT. In order to further a close working relationship, the Parties will provide offices and support to each other at each other's facilities for the visiting personnel of the other Party, as provided herein. During the Research Period, each Party shall provide employees at the other Party's facilities, on an as-needed basis to be determined by the RMC. In addition, the RMC shall arrange for routine visits by other Rigel personnel to Janssen facilities to facilitate information exchange between the Parties.

4. INTERNAL JANSSEN RESEARCH

4.1 TECHNOLOGY TRANSFER. During the Research Period, Janssen will periodically notify Rigel of the Rigel Technology Assays and other assays that are part of the Janssen Internal Research which Janssen or its permitted sublicensees choose to pursue. Promptly thereafter, Rigel and Janssen shall meet to determine whether the Rigel Technology Assays and such other assays described in such notice are within the scope of Internal Janssen Research. If the Parties determine that such assays are within the scope of the Internal Janssen Research, Rigel shall transfer the Rigel Technology Assays to Janssen or its permitted sublicensees, and shall provide such reasonable assistance as is necessary to establish functioning assays, such assistance to be included in the 10 FTE's that Rigel is required to allocate to the Research Program. For the avoidance of any doubt, any Rigel Technology Assays transferred, and any information shared with Janssen or its permitted sublicensees in connection with the Internal Janssen Research shall be used by Janssen or its permitted sublicensees only to the extent of the licenses granted to Janssen under Section 5.4.

4.2 USE OF RIGEL ASSAYS. Janssen shall use the Rigel Technology Assays for the Internal Janssen Research only, and shall not transfer or otherwise grant access to such assays to any Affiliate or Third Party, other than to permitted sublicensees pursuant to Section 5.4.

4.3 REPORTING. Janssen shall provide Rigel with written reports on the Internal Janssen Research and the use of the Rigel Technology Assays not less than once every calendar year.

5. LICENSE GRANTS; CONFLICTING PROGRAMS; DILIGENCE

5.1 LICENSE GRANTS FOR COLLABORATIVE RESEARCH.

(a) GRANT BY RIGEL. Rigel hereby grants to Janssen and its Affiliates a nonexclusive, non-transferable, royalty-free license in the Field of Research during the Research Period under the Rigel Technology, and Rigel's interest in the Research Program Technology in the Territory, subject to the terms of this Agreement, solely for the purpose of carrying out Janssen's responsibilities under the Research Program.

(b) GRANT BY JANSSEN. Janssen hereby grants to Rigel and its Affiliates a nonexclusive, non-transferable, royalty-free license in the Field of Research during the Research Period under the Janssen Technology and Janssen's interest in the Research Program Technology in the Territory, subject to the terms of this Agreement, solely for the purpose of carrying out Rigel's responsibilities under the Research Program.

5.2 COMMERCIAL LICENSE GRANT. Subject to the terms and conditions of this Agreement, Rigel hereby grants to Janssen and its Affiliates an exclusive, royalty-bearing license, with the right to grant sublicenses, under the Rigel Technology and Rigel's interest in the Research Program Technology, to discover, develop, identify, make, have made, use, sell, have sold, offer for sale, export, and import Products in the Territory.

5.3 COMMERCIAL DUE DILIGENCE. The rights granted under Section 5.2 shall be subject to Janssen's obligation to discover, develop and commercially exploit Products using the level of effort commensurate with other Janssen products at a similar stage of development and of similar importance (based on criteria such as patient population, price per treatment and competitive position). If Janssen fails to use such diligence, Rigel may notify Janssen of such failure and, if not cured within six (6) months of such notice, terminate the license under Section 5.2 with respect to such Product.

5.4 LICENSE FOR INTERNAL JANSSEN RESEARCH. Rigel hereby grants Janssen a non-exclusive, worldwide, royalty bearing license, during the Term of Agreement under the Rigel Technology and Rigel's interest in the Research Program Technology to the extent necessary to use the Rigel Technology Assays for the Internal Janssen Research. Janssen shall have the right to grant sublicenses under the license granted under this Section 5.4 to The R.W. Johnson Pharmaceutical Research Institute, a Division of Ortho-McNeil Pharmaceutical, Inc., and subject to Rigel's prior approval (which approval shall not be unreasonably withheld) to other named Affiliates; PROVIDED, HOWEVER, that any such sublicense shall provide for a license to Rigel corresponding to the license granted by Janssen to Rigel under Section 5.5, and shall be subject and subordinate to the terms of this Agreement. Janssen shall provide Rigel with a copy of each sublicense agreement.

5.5 LICENSE TO RIGEL OF IMPROVEMENTS TO RIGEL TECHNOLOGY. Janssen hereby grants to Rigel a nonexclusive, royalty-free, paid-up, worldwide license (i) under Janssen's interest in all Research Program Technology, and (ii) under Janssen's interest in any know-how, inventions or discoveries generated or made in the course of the Internal Janssen Research, only to the extent it constitutes an improvement of Rigel Technology.

5.6 EXCLUSIVITY PERIOD. During the first 18 months after the Effective Date, Rigel will not enter into a research collaboration with a Third Party ("Third Party Collaboration") in the Field of Research (the "Exclusive Research Period").

5.7 CONFLICTING PROGRAMS.

(a) After the Exclusive Research Period and during the Research Period, Rigel will notify Janssen if it has decided to pursue a research project in human oncology described in such notice ("Additional Program"). Within sixty (60) days after receipt of Rigel's notice, the Parties shall determine whether or not the Additional Program conflicts with the Research Program. An Additional Program will be considered to conflict with the Research Program if, after consultation with the RMC, the VP Biological Research of Janssen and the CEO of Rigel agree that there is significant overlap between the molecular targets or pathways of the Additional Program and the Field of Research.

(b) If such a conflict is determined to exist then (i) Rigel shall not proceed with the Additional Program, and (ii) Janssen may notify Rigel within sixty (60) days of such determination of its interest in such Additional Program. If Janssen so notifies Rigel, then the Parties will enter

into good faith discussions to determine whether there are mutually agreeable terms upon which they wish to collaborate with respect to the Additional Program. If Janssen does not so notify Rigel or if the Parties do not enter into an agreement with respect to the Additional Program within ninety (90) days (or such further period as the Parties may agree) after Janssen's notice, then such Additional Program shall not be added to the Research Program.

(c) If such a conflict is determined not to exist, Janssen may notify Rigel within sixty (60) days of such determination of its interest in such Additional Program. If Janssen so notifies Rigel, then the Parties will enter into good faith discussions to determine whether there are mutually agreeable terms upon which they wish to collaborate with respect to the Additional Program. If Janssen does not so notify Rigel or if the Parties do not enter into an agreement with respect to the Additional Program within ninety (90) days (or such further period as the Parties may agree) after Janssen's notice, then Rigel shall be free to pursue the Additional Program alone or with a Third Party; PROVIDED, HOWEVER, that Rigel shall not enter into any agreement with a Third Party on terms which are substantially the same or less favorable to Rigel, than the terms last offered by Janssen to Rigel in writing.

5.8 SUBLICENSES UNDER STANFORD AGREEMENTS. Subject to Section 6.15 (Third Party Payments by Rigel), the Parties hereby acknowledge that the Stanford Required Provisions are included in this Agreement for the benefit of Stanford University. The sublicenses granted hereunder shall remain in effect after termination of the Stanford Agreements, provided that any obligations of Janssen under the sublicenses granted herein shall be owed to Stanford.

6. FINANCIAL SUPPORT

6.1 SIGNING PAYMENT. Within ten (10) days of the Effective Date of this Agreement, Janssen will pay Rigel One Million US Dollars (US$1,000,000).

6.2 RESEARCH SUPPORT. Janssen will provide funding to support Rigel's efforts under the Research Program and 10 FTE'S of Rigel at a rate of US$2,500,000 per year. Such amount shall be paid quarterly in advance.

6.3 PAYMENTS FOR PHARMACEUTICAL COLLABORATION PRODUCTS.

(a) MILESTONE PAYMENTS. For Pharmaceutical Collaboration Products, the following payments will be due to Rigel upon the occurrence of the following events:

<TABLE>
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MILESTONE EVENT	AMOUNT OF PAYMENT
<S>	<C>
1) First to occur of either (a) Janssen initiating compound screening with the second Validated Target-Peptide Pair delivered by Rigel or (b) six (6) months after Rigel delivers the second Validated Target-Peptide Pair.	$500,000
2) Demonstration by Janssen of IN VIVO efficacy in at least one animal model of the first Pharmaceutical Collaboration Product identified in a screening assay using a Janssen Collaboration Target.	$500,000
3) Selection by Janssen of the first Development Candidate.	$1 million
4) Enrollment of the fifth patient in a Phase III Clinical Trial for the first Pharmaceutical Collaboration Product	$2 million
5) Approval of the first NDA for each Pharmaceutical Collaboration Product in the first Major Market.	$5 million

</TABLE>

(b) ROYALTIES. Janssen shall pay Rigel royalties on Net Sales of Pharmaceutical Collaboration Products at a rate of four percent (4%)

when the Pharmaceutical Collaboration Product contains a compound originating from Janssen's compound collection and six percent (6%) when the Pharmaceutical Collaboration Product contains a compound originating from Rigel's compound collection.

6.4 PAYMENTS FOR TARGET-PEPTIDE THERAPEUTIC PRODUCTS.

(a) MILESTONE PAYMENTS. For Target-Peptide Therapeutic Products, the following payments will be due to Rigel upon the occurrence of the following events:

MILESTONE EVENT	AMOUNT OF PAYMENT
1) Demonstration by Janssen of in vivo efficacy in at least one animal model of the first Target-Peptide Therapeutic Product.	$500,000
2) Selection by Janssen of the first Development Candidate.	$1 million

3) Enrollment of the fifth patient in a Phase III Clinical Trial for the first Target-Peptide Therapeutic Product	$2 million
4) Approval of the first NDA for each Target-Peptide Therapeutic Product in the first Major Market.	$5 million

(b) ROYALTIES. Janssen shall pay Rigel royalties on Net Sales of Target-Peptide Therapeutic Products at a rate of six percent (6%).

6.5 PAYMENTS FOR DIAGNOSTIC PRODUCTS.

(a) MILESTONE PAYMENTS. For Diagnostic Products, the following payment will be due to Rigel upon the occurrence of the following event:

MILESTONE EVENT	AMOUNT OF PAYMENT
1) Regulatory Approval of the first Diagnostic Product derived from each VTPP	$500,000.00

(b) ROYALTIES. Janssen shall pay Rigel royalties on Net Sales of Diagnostic Products at a rate of two percent (2%) when the Diagnostic Product is patented, and one percent (1%) when the Diagnostic Product is not patented.

6.6 PAYMENTS FOR NON-COLLABORATION PHARMACEUTICAL PRODUCTS.

(a) MILESTONE PAYMENTS. For Non-Collaboration Pharmaceutical Products, the following payments will be due to Rigel upon the occurrence of the following events:

MILESTONE EVENT	AMOUNT OF PAYMENT
1) Enrollment of the fifth patient in a Phase III Clinical Trial for the first Non-Collaboration Pharmaceutical Product	$1 million
2) Approval of the first NDA for the first Non-Collaboration Pharmaceutical Product in the first Major Market.	$2.5 million

</TABLE>

(b) ROYALTIES. Janssen shall pay Rigel royalties on Net Sales of Non-Collaboration Pharmaceutical Products at a rate of two percent (2%).

6.7 ROYALTY PERIOD.

(a) In respect of Products for which a royalty is due, Janssen's obligation to pay royalties to Rigel shall be for a period of ten (10) years, on a Product-by-Product basis, from the Date of First Sale of each such Product.

(b) For the purposes of determining whether royalties are due hereunder, different dosage forms of a Product shall not be considered different Products provided that different dosage forms contain the same active ingredient.

(c) Upon termination of the royalty payment obligation, Janssen shall thereafter have in perpetuity a royalty-free, non-exclusive license to make, have made, use, sell, have sold, and import such Products hereunder, without any accounting to Rigel.

6.8 MANNER OF PAYMENT. Remittance of payments under this Article 6 shall be made by means of wire transfer or other telegraphic transfer in U.S. Dollars to Rigel's account in a bank in the United States to be designated from time to time by Rigel.

6.9 REPORTS. Janssen shall provide written notice of the occurrence of all milestone events in this Article. Within forty-five (45) days following each quarterly period of a calendar year after the Date of First Sale of the first Product, Janssen shall render to Rigel a written report setting forth the Net Sales of such Products sold and the royalty due and payable on a Product-by-Product and country-by-country basis (including all deductions taken from the gross sales price in determining Net Sales).

6.10 INVOICING. All payments to be made by Janssen under this Agreement shall be made based upon an invoice to be submitted by Rigel to Janssen. The invoice shall be in the form attached hereto as Exhibit C. Except as otherwise provided in Section 6.1, all payments shall be due within fifteen (15) days of the receipt of such invoice by Janssen.

6.11 RECORDS AND AUDIT.

(a) During the term of this Agreement and for a period of at least two (2) years thereafter, Janssen shall keep complete and accurate records pertaining to the sale or other disposition of the Products commercialized by it, in sufficient detail to permit Rigel to confirm the accuracy of all payments due hereunder.

(b) Rigel shall have the right to cause an independent, certified public accountant acceptable to Janssen to audit such records to confirm Janssen's Net Sales of Products and royalty payments made under this Agreement; PROVIDED, HOWEVER, that such auditor shall not disclose Janssen's confidential information to Rigel, except to the extent such disclosure is necessary to verify the amount of royalties due under this Agreement. Such audits may be exercised once a year, within two (2) years after the royalty period to which such records relate, upon prior written notice to Janssen and during normal business hours. Rigel shall bear the full cost of such audit unless such audit discloses an understatement of more than five percent (5%) from the amount of the Net Sales or royalties previously paid. In such case, Janssen shall bear

the full cost of such audit. In case that such audit discloses an overpayment of royalties by Janssen, such overpayment shall be refunded to Janssen. The terms of this Section 6.11 shall survive any termination or expiration of this Agreement for a period of two (2) years.

6.12 FOREIGN EXCHANGE. The remittance of royalties payable on Net Sales will be payable in U.S. dollars to Rigel at a bank and to an account designated by Rigel using a rate of exchange of the currency of the country from which the royalties are payable in accordance with the currency exchange

rates as published in the Wall Street Journal at the end of the calendar quarter in which the Net Sales were made. All references to dollars herein are references to U.S. dollar.

6.13 BLOCKED CURRENCY. Where royalties are due for Net Sales in a country where by reason of currency regulations of any kind it is impossible to make royalty payments for that country's Net Sales said royalties shall be deposited in whatever currency is allowable for the benefit or credit of Rigel in any accredited bank in that country as shall be acceptable to Rigel. Moreover, when necessary to facilitate payments from countries other than the United States, when requested by Janssen, Rigel shall enter into direct license agreements with Janssen Affiliates designated by Janssen, whereby such Affiliate will be obligated to remit royalty payments due for Net Sales in such country directly to Rigel. Each such license agreement shall contain substantially the same terms as this Agreement insofar as such terms are lawful under applicable laws and regulations of the particular country; and Janssen shall be responsible for the performance of all obligations of Janssen Affiliates under such license agreements.

6.14 TAXES. All payments under this Agreement will be made without any deduction or withholding for or on account of any tax unless such deduction or withholding on behalf of Rigel is required by any applicable law. If Janssen is so required to deduct or withhold, Janssen will:

(a) promptly notify Rigel of such requirement;

(b) pay to the relevant authorities the full amount required to be deducted or withheld promptly upon the earlier of determining that such deduction or withholding is required or receiving notice that such amount has been assessed against Rigel;

(c) promptly forward to Rigel an official receipt (or certified copy), or other documentation reasonably acceptable to Rigel, evidencing such payment to such authorities.

6.15 THIRD PARTY PAYMENTS BY RIGEL. All payments due to Third Parties pursuant to agreement between Rigel and a Third Party that relate to Rigel Technology shall be made by and or the account of Rigel. Janssen assumes no responsibility for any payment due to Stanford University, the State University of New York at Stony Brook, BASF, any other Third Party pursuant to an agreement between Rigel and such Third Party.

7. INTELLECTUAL PROPERTY

7.1 INFORMATION AND REPORTS. The Parties will provide to the RMC promptly and at least quarterly the results of the research activities conducted in the Research Program, such reports to be in such form as specified by the RMC. The Parties shall keep complete and accurate records pertaining to the results of work conducted pursuant to the Research Program. Such records shall be maintained for a period of at least five (5) years following the year in which any such efforts were made hereunder; PROVIDED, HOWEVER, that all laboratory notebooks pertaining to the result of the work conducted pursuant to the Research Program shall be maintained for at least twenty (20) years.

7.2 DISCLOSURE OF PATENTABLE INVENTIONS. In addition to the disclosures required, each Party shall provide the other any invention disclosure related to the Research Program which has been submitted to it in the normal course of disclosing an invention. Such invention disclosures shall be provided promptly after submission and in no event later than 10 business days after the end of the calendar quarter in which the disclosure was submitted.

7.3 OWNERSHIP OF RESEARCH PROGRAM KNOW-HOW; INVENTIONS. Except as otherwise set forth herein, Research Program Know-How (including, without limitation, any patentable invention or discovery) acquired, developed or made solely by employees of one Party during the course of the Research Program ("Sole Inventions") shall be the property of such Party. Research Program Know-How (including, without limitation, any patentable invention or discovery) acquired, developed or made jointly by employees of Janssen and Rigel as determined in accordance with United States rules of inventorship, shall be owned jointly by Janssen and Rigel, each to own an undivided one-half (1/2) interest in such Research Program Know-How ("Joint Invention") except as provided and subject to the licenses granted herein. Each Party shall cooperate with the other in completing any patent applications relating to Joint Inventions, and in executing and delivering any instrument required to assign, convey or transfer to such other Party its undivided one-half (1/2) interest.

7.4 PATENT PROSECUTION. Each Party will prepare, file, prosecute and maintain patent applications for its Sole Inventions and shall be responsible for related interference proceedings. The Parties will endeavor to ensure that such patent applications are filed before any public disclosure by either Party to maintain the validity of patent applications to be filed outside of the United States and to comply with the provisions of Article 9. Janssen shall be responsible for filing and prosecuting applications for, and maintaining, Joint Inventions not related to Rigel Technology, using counsel of its choice, throughout the world. Janssen shall pay all expenses for filing applications for, and maintenance of, such Joint Inventions. In the event that a Party decides not to proceed with filing or prosecuting an application for, or maintaining, a Research Program Patent for which it is responsible under this Section 7.3, it shall give the other Party ninety (90) days written notice before any public disclosure or any relevant prosecution or maintenance deadline and transmit all information reasonable and appropriate relating to such Research Program Patent, and such other Party shall have the right to pursue, at its own expense, prosecution of such application for, or maintenance of, such patent.

7.5 INFRINGEMENT BY THIRD PARTIES.

(a) NOTICE. Each Party shall promptly notify the other in writing of any alleged or threatened infringement of the Research Program Patents, which may adversely impact the rights of the Parties hereunder, of which it becomes aware.

(b) ENFORCEMENT ACTION. In the event that the Parties become aware of any alleged or threatened infringement of the Research Program Patents, other than Research Program Patents relating to Rigel Technology, Janssen shall have the right, but not the obligation, to take appropriate action against any person or entity directly or contributorily infringing such Research Program Patent. In the event Janssen fails to institute an infringement suit or take other reasonable action in response to such infringement within sixty (60) days, Rigel shall have the right, but not the obligation upon thirty (30) days written notice to Janssen, to institute such suit or take other appropriate action in its own name, the joint owner's name, or both. Rigel shall have the right, but not the obligation, to take appropriate action against any person or entity directly or contributorily infringing a Research Program Patent relating to Rigel Technology. In the event Rigel fails to institute an infringement suit or take other reasonable action in response to such infringement within sixty (60) days, Janssen shall have the right, but not the obligation upon thirty (30) days notice to Rigel, to institute such suit or take other appropriate action in its own name, the joint owner's name, or both. Regardless of which Party brings an enforcement action, the other Party hereby agrees to cooperate reasonably in any such effort, including, if required, furnishing a power of attorney. The Party not bringing the action shall have the right to participate in such action at its own expense with its own counsel and in such case any recovery obtained by settlement or otherwise shall be shared by the Parties in accordance with their economic interests in such Research Program Patent.

7.6 INFRINGEMENT OF THIRD PARTY PATENT RIGHTS.

(a) JOINT STRATEGY. In the event that the use or sale of a Product becomes the subject of a claim of infringement of a patent, copyright or other proprietary right anywhere in the world, and without regard to which Party is charged with said infringement, and the venue of such claim, the Parties shall promptly confer to discuss the claim.

(b) DEFENSE. Unless the Parties otherwise agree, Janssen shall assume the primary responsibility for the conduct of the defense of any such claim. Rigel shall have the right, but not the obligation, to participate in any such suit at its sole option and at its own expense. Each Party shall reasonably cooperate with the Party conducting the defense of the claim. Neither Party shall enter into any settlement that affects the other party's rights or interests without such other party's written consent, not to be unreasonably withheld.

8. REPRESENTATIONS AND WARRANTIES

8.1 REPRESENTATIONS AND WARRANTIES. Each Party represents and warrants to the other that:

(a) CORPORATE POWER. It is duly organized and validly existing under the laws of its state or country of incorporation, and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof.

(b) DUE AUTHORIZATION. It is duly authorized to execute and deliver this Agreement and to perform its obligations hereunder, and the person or persons executing this Agreement on its behalf has been duly authorized to do so by all requisite corporate action.

(c) BINDING AGREEMENT. This Agreement is legally binding upon it and enforceable in accordance with its terms. The execution, delivery and performance of this Agreement by it does not conflict with any agreement, instrument or understanding, oral or written, to which it is a Party or by which it may be bound, nor violate any material law or regulation of any court, governmental body or administrative or other agency having jurisdiction over it.

(d) GRANT OF RIGHTS; MAINTENANCE OF AGREEMENTS. It has not, and will not during the term of this Agreement, grant any right to any Third Party which would conflict with the rights granted to the other Party hereunder. It has (or will have at the time performance is due) maintained and will maintain and keep in full force and effect all agreements necessary to perform its obligations hereunder.

(e) VALIDITY. It is aware of no action, suit or inquiry or investigation instituted by any governmental agency, which questions or threatens the validity of this Agreement.

(f) EMPLOYEE OBLIGATIONS. All of its employees, officers and consultants have executed agreements requiring in the case of employees and officers, assignment to the Party of all inventions made during the course of and as a result of their association with such Party and obligating the individual to maintain as confidential the confidential information of the Party, as well as the confidential information of a Third Party which such Party may receive.

(g) PERFORMANCE BY AFFILIATES. The Parties recognize that each may perform some or all of its obligations under this Agreement through Affiliates, provided, however, that each Party shall remain responsible and be guarantor of the performance by its Affiliates and shall cause its Affiliates to comply with the provisions of this Agreement in connection with such performance.

8.2 WARRANTY AND DISCLAIMER CONCERNING TECHNOLOGY. As of the Effective Date of this Agreement, it is not aware of any Third Party patents that would prevent the other Party from exercising the licenses granted herein, or would prevent a Party from carrying out the Research Program. NOTWITHSTANDING THE FOREGOING, THE TECHNOLOGY PROVIDED BY EACH PARTY HEREUNDER IS PROVIDED "AS IS" AND EACH PARTY EXPRESSLY DISCLAIMS ANY AND ALL WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION THE WARRANTIES OF DESIGN, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, NONINFRINGEMENT

OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES OR ARISING FROM A COURSE OF DEALING, USAGE OR TRADE PRACTICES, IN ALL CASES WITH RESPECT THERETO. Without limiting the generality of the foregoing, each Party expressly does not warrant (i) the success of any research commenced under the Research Program or (ii) the safety or usefulness for any purpose of the technology it provides hereunder.

9. CONFIDENTIALITY; PUBLICATION

9.1 CONFIDENTIALITY. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing by the Parties, the Parties agree that, for the term of this Agreement and for five (5) years thereafter, the receiving Party (the "Receiving Party") shall keep confidential and shall not publish or otherwise disclose and shall not use for any purpose other than as provided for in this Agreement any Confidential Information furnished to it by the other Party (the "Disclosing Party") pursuant to this Agreement unless the Receiving Party can demonstrate by contemporaneous, competent written proof that such Confidential Information:

(a) was already known to the Receiving Party, other than under an obligation of confidentiality, at the time of disclosure by the Disclosing Party;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the Receiving Party in breach of the Agreement;

(d) was disclosed to the Receiving Party, other than under an obligation of confidentiality to a Third Party, by a Third Party who had no obligation to the Disclosing Party or any Third Party not to disclose such information to others; or

(e) was independently discovered or developed by the Receiving Party without the use of Confidential Information belonging to the Disclosing Party.

9.2 AUTHORIZED DISCLOSURE. Each Party may disclose Confidential Information belonging to the other Party to the extent such disclosure is reasonably necessary in the following instances:

(a) filing or prosecuting patents relating to Research Program Technology;

(b) regulatory filings;

(c) prosecuting or defending litigation;

(d) complying with applicable governmental regulations;

(e) conducting pre-clinical or clinical trials of Products; and

(f) disclosure to Affiliates, sublicensees, employees, consultants or agents who agree to be bound by similar terms of confidentiality and non-use at least equivalent in scope to those set forth in this Article 9.

Notwithstanding the foregoing, in the event a Party is authorized to make a disclosure of the other party's Confidential Information pursuant to this Section 9.2 it will, except where impracticable, give reasonable advance notice to the other Party of such disclosure and use reasonable efforts to secure confidential treatment of such information. In any event, the Parties agree to take all reasonable action to avoid disclosure of Confidential Information hereunder. The Parties will consult with each other concerning the provisions of this Agreement to be redacted in any filings made by the Parties with the Securities and Exchange Commission or as otherwise required by law.

9.3 PUBLICATIONS.

(a) REVIEW AND APPROVAL. Each Party to this Agreement recognizes that the publication of papers, including oral presentations and abstracts, regarding the Research Program Know-How and the Research Program Patents, subject to reasonable controls to protect Confidential Information, will be beneficial to both Parties. However, each Party shall have the right to review and approve any paper proposed for publication by the other Party or its permitted sublicensees, including oral presentations and abstracts, which utilizes data generated from the Research Program and/or includes Research Program Know-How or Confidential Information of the reviewing Party.

(b) REVIEW AND APPROVAL PROCESS. At least thirty (30) days before any such paper is presented or submitted for publication, the Party or its permitted sublicensee proposing publication shall deliver a complete copy to the other Party. The receiving Party shall review any such paper and give its comments to the publishing Party or its permitted sublicensee within thirty (30) days of the delivery of such paper to the receiving Party. With respect to oral presentation materials and abstracts, the Parties shall make reasonable efforts to expedite review of such materials and abstracts, and shall return such items as soon as practicable to the publishing Party with appropriate comments, if any, but in no event later than thirty (30) days from the delivery date thereof to the receiving Party. The publishing Party or its permitted sublicensee shall comply with the other Party's request to delete references to such other Party's Confidential Information in any such paper and agrees to withhold publication of same an additional ninety (90) days in order to permit the Parties to file patent application, if either of the Parties deem it necessary, in accordance with the terms of this Agreement.

9.4 PUBLICITY. Neither Party shall, without the prior written consent of the other Party (which consent shall not be unreasonably withheld or delayed), originate any publicity, news release or public announcement, written or oral, whether to the public or press, relating to this Agreement, including its existence, the subject matter to which it relates, performance under it or any of its terms or to any amendment hereto, excepting only such announcements as in the opinion of counsel for the Party making such announcement is required by law to be made. Any such announcements shall be factual and as brief as

possible. If a Party decides to make an

announcement required by law, it will give the other Party 10 business days' advance written notice, where possible, of the text of the announcement so that the other Party will have an opportunity to comment upon the announcement. To the extent that the receiving Party requests that any information in the materials proposed to be disclosed be deleted, the disclosing Party shall request confidential treatment of such information pursuant to any applicable rules or regulations (including those of the Securities and Exchange Commission) relating to the confidential treatment of such information so that there be omitted from the materials that are proposed to be disclosed any information that the receiving Party reasonably requests to be deleted. The Parties shall mutually agree upon a press release to be made on or promptly after the Effective Date. Any information which has been disclosed to Third Parties pursuant to this Section 9.4 may be repeated in whole or in part in any subsequent disclosures or statements to Third Parties without the restrictions contained herein.

10. TERM AND TERMINATION

10.1 TERM OF THE AGREEMENT. This Agreement shall become effective upon the Effective Date and continue, unless earlier terminated pursuant to Section 10.2 or 10.3, until the expiration of the last to expire patent claiming a Product (the "Term of Agreement").

10.2 EARLY TERMINATION. This Agreement shall terminate upon thirty (30) days prior notice by Rigel (a) if Janssen has not selected a Preliminary Target-Peptide Pair for further evaluation pursuant to Section 3.4 prior to the expiration of the Research Period or, (b) if Janssen does not initiate compound screening as provided in Section 3.6 prior to the expiration of the latest to expire Exclusivity Term.

10.3 TERMINATION FOR BREACH. In the event that (a) either Party shall commit a material breach at any time and (b) such defaulting Party shall fail to remedy such material breach within sixty (60) days after the date of notice thereof by the non-defaulting Party to the defaulting Party (or, if such material breach cannot be remedied within sixty (60) days, such longer period of time as may be reasonably necessary provided the defaulting Party commences to remedy such material breach within such sixty (60) day period and thereafter proceeds promptly and diligently to complete such remedy) (with respect to the defaulting Party, an "Event of Default"), then the non-defaulting Party may at any time thereafter terminate this Agreement.

10.4 JANSSEN REMEDIES UPON TERMINATION. If this Agreement is terminated as a result of an Event of Default by Rigel, the licenses granted in Article 5 herein shall survive such termination. In such event, Janssen's obligations in Article 6 shall survive, except that all royalty rates shall be reduced by fifty percent.

10.5 RIGEL CHANGE OF CONTROL.

(a) If a Rigel Change of Control (as defined below) occurs during the Research Period, then Janssen shall have the right, in its sole discretion, to terminate the Research Program and the Research Period by giving thirty (30) days' prior written notice thereof

to Rigel at any time during the sixty (60) day period following the occurrence of the Rigel Change of Control. Upon such termination by Janssen pursuant to this subsection (a), then:

(i) all unspent research funds paid to Rigel pursuant to Section 6.2 shall be returned promptly to Janssen; and

(ii) Rigel shall have no further obligation to transfer VTPPs or Rigel Technology Assays, or provide other assistance to Janssen for Internal Janssen Research;

(iii) Section 2, 3 (except for Sections 3.6 (Compound Screening; Diligence) and 3.7 (Additional Janssen Right to Validated Target-Peptide Pair), 5.1, 5.6, 5.7, and 7.2 shall terminate;

(iv) all other terms and conditions of this Agreement shall continue in full force and effect.

(b) For the purpose of this Section 10.5, a "Rigel Change of

Control" shall have occurred only at such time as a Third Party with (i) annual sales of pharmaceutical and diagnostic products of more than one billion dollars, and (ii) a market capitalization of more than fifteen billion dollars acquires, in one transaction or a series of transactions, either (y) all or substantially all of the assets of Rigel, or (z) more than 50% of the outstanding voting securities of Rigel (whether by stock acquisition, merger or otherwise).

10.6 TERMINATION NOT SOLE REMEDY. Termination is not the sole remedy under this Agreement, and, whether or not termination is effected, all other remedies will remain available except as agreed to otherwise herein (including, without limitation, any remedies in favor of Janssen referred to in Paragraph 10.5).

11. INDEMNITY

11.1 RESEARCH AND DEVELOPMENT INDEMNIFICATION. Each Party (the "Indemnifying Party") shall indemnify, defend and hold the other Party (the "Indemnified Party") harmless from and against any and all liabilities, claims, damages, costs, expenses or money judgments incurred by or rendered against the Indemnified Party and its Affiliates and sub-licensees incurred in the defense or settlement of a Third Party lawsuit or in a satisfaction of a Third Party judgment arising out of any injuries to person and/or damage to property resulting from (a) negligence of the Indemnifying Party performed in carrying out the development program hereunder, and (b) personal injury to the Indemnified Party's employees or agents or damage to the Indemnified Party's property resulting from acts in carrying out activities contemplated by this Agreement.

11.2 PRODUCT LIABILITY. Janssen hereby agrees to indemnify, hold harmless and defend Rigel and its directors, officers, employees, and agents against any claim or claims, including, but not limited to liability, suits, actions, demands, expenses and/or loss including reasonable legal expenses and attorneys fees, arising from bodily injury and death, resulting from or arising out of the manufacture, use or sale of Products by Janssen, its Affiliates and sub-licensees.

11.3 CONTROL OF DEFENSE. Any entity entitled to indemnification under this Article shall give notice to the indemnifying Party of any Claims that may be subject to indemnification, promptly after learning of such Claim, and the indemnifying Party shall assume the defense of such Claims with counsel reasonably satisfactory to the indemnified Party. If such defense is assumed by the indemnifying Party with counsel so selected, the indemnifying Party will not be subject to any liability for any settlement of such Claims made by the indemnified Party without its consent (but such consent will not be unreasonably withheld or delayed), and will not be obligated to pay the fees and expenses of any separate counsel retained by the indemnified Party with respect to such Claims.

12. GOVERNING LAW; DISPUTE RESOLUTION

12.1 GOVERNING LAW. This Agreement shall be governed by Delaware law, as such law applies to contracts entered into in Delaware by residents of Delaware.

12.2 COMPLIANCE WITH LAWS. The Parties shall comply with all applicable laws, rules, regulations and orders of the United States and all jurisdictions and any agency or court thereof in connection with this Agreement and the transactions contemplated thereby.

12.3 DISPUTE RESOLUTION. Except as provided in Section 2.3 above, in the event of a dispute, the Parties shall refer such dispute to a designated executive of Rigel and a designated executive of Janssen for attempted resolution by good faith negotiations within thirty (30) days after such referral is made. In the event such executives are unable to resolve such dispute within such thirty (30) day period, either Party may invoke the provisions of Section 12.4 below.

12.4 JURISDICTION AND VENUE. Except as provided in Section 2.3 and 12.3 above, any claim or controversy arising out of or related to this Agreement or any breach hereof shall be adjudicated in the state and federal courts having jurisdiction over disputes arising in the State of Delaware, and the Parties hereby consent to the jurisdiction and venue of such court.

13. PRODUCT DEVELOPMENT AND COMMERCIALIZATION

13.1 JANSSEN'S DEVELOPMENT RESPONSIBILITIES. Janssen shall be solely responsible for and have the sole right to select a compound for development into a Product. Once such a compound is selected for development, Janssen shall

be solely responsible for and shall have the sole right to develop such compound throughout Pre-phase I and Phases I, II and III including making all Drug Approval Applications and obtaining all Regulatory Approvals on a worldwide basis. In this regard, Janssen agrees to carry out development of such compound consistent with its normal business practices. This development effort shall include the right to slow or terminate development and all other actions deemed by Janssen to be reasonable in the development of the compound. Moreover, Janssen shall be responsible for all cost and expenses in connection with such development efforts.

13.2 MARKETING OBLIGATIONS. All business decisions, including, but not limited to, the design, sale, price and promotion of Products under this Agreement and the decision whether to market any particular Product shall be within the sole discretion of Janssen. Any marketing of a

Product in one market or country shall not obligate Janssen to market said Product in any other market or country. Furthermore Janssen makes no representation or warranty that the market of a Product shall be the exclusive means by which Janssen will participate in any therapeutic field.

14. GENERAL PROVISIONS

14.1 NOTICES. All notices required or permitted to be given under this Agreement shall be in writing and shall be mailed by registered or certified mail addressed to the signatory to whom such notice is required or permitted to be given and transmitted by facsimile to the number indicated below. All notices shall be deemed to have been given when mailed, as evidenced by the postmark at the point of mailing, or faxed; provided that such fax is confirmed by electronic confirmation of transmission.

All notices to Janssen shall be addressed as follows:

Janssen Pharmaceutica N.V.
Turnhoutseweg 30
2340 Beerse, BELGIUM
Attention: Executive Vice President
Fax: (32+14) 60-28-41

with a copy to:

Office of General Counsel
Johnson & Johnson
One Johnson & Johnson Plaza
New Brunswick, New Jersey 08933 U.S.A.,
Telephone (732) 524-2485,
Telecopy (732) 524-2788

All notices to Rigel shall be addressed as follows:

Rigel Pharmaceuticals, Inc.
772 Lucerne Drive
Sunnyvale, California 94086
Attn: President
Fax: (408) 736-1588

with a copy to:

Cooley Godward LLP
Five Palo Alto Square
3000 El Camino Real
Palo Alto, California 94306
Attn: Robert L. Jones, Esq.
Fax: (650) 857-0663

Any Party may, by written notice to the other, designate a new address or fax number to which notices to the Party giving the notice shall thereafter be mailed or faxed.

14.2 FORCE MAJEURE. No Party shall be liable for any delay or failure of performance to the extent such delay or failure is caused by circumstances beyond its reasonable control and that by the exercise of due diligence it is unable to prevent, provided that the Party claiming excuse uses its best efforts

to overcome the same.

14.3 ENTIRETY OF AGREEMENT. This Agreement embodies the entire, final and complete agreement and understanding between the Parties and replaces and supersedes all prior discussions and agreements between them with respect to its subject matter. No modification or waiver of any terms or conditions hereof shall be effective unless made in writing and signed by a duly authorized officer of each Party.

14.4 NON-WAIVER. The failure of a Party in any one or more instances to insist upon strict performance of any of the terms and conditions of this Agreement shall not constitute a waiver or relinquishment, to any extent, of the right to assert or rely upon any such terms or conditions on any future occasion.

14.5 DISCLAIMER OF AGENCY. Neither Party is, or will be deemed to be, the legal representative or agent of the other, nor shall either Party have the right or authority to assume, create, or incur any Third Party liability or obligation of any kind, express or implied, against or in the name of or on behalf of another except as expressly set forth in this Agreement.

14.6 SEVERABILITY. If a court of competent jurisdiction declares any provision of this Agreement invalid or unenforceable, or if any government or other agency having jurisdiction over either Rigel or Janssen deems any provision to be contrary to any laws, then that provision shall be severed and the remainder of the Agreement shall continue in full force and effect. To the extent possible, the Parties shall revise such invalidated provision in a manner that will closely approximate the parties' original intent.

14.7 AFFILIATES; ASSIGNMENT. Except as otherwise provided herein, neither Party may assign its rights or delegate its duties under this Agreement without the prior written consent of the other Party, not to be unreasonably withheld; PROVIDED, HOWEVER, that either Party may assign this Agreement to any of its Affiliates or to any successor by merger or sale of substantially all of its business unit to which this Agreement relates in a manner such that the assignor will remain liable and responsible for the performance and observance of all its duties and obligations hereunder. This Agreement shall be binding upon the successors and permitted assigns of the Parties. Any attempted delegation or assignment not in accordance with this Section 14.7 shall be of no force or effect

14.8 HEADINGS. The headings contained in this Agreement have been added for convenience only and shall not be construed as limiting.

14.9 COUNTERPARTS. This Agreement may be executed in one or more counterparts, each of which shall be an original and all of which shall constitute together the same document.

14.10 ENGLISH LANGUAGE. This Agreement has been prepared in the English language and shall be construed in the English language.

14.11 LICENSOR BANKRUPTCY. All rights and licenses granted under or pursuant to this Agreement by Rigel to Janssen are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11, U.S. Code (the "Bankruptcy Code"), licenses of rights to "intellectual property" as defined under section 101(60) of the Bankruptcy Code. The Parties agree that Janssen, as a licensee of such rights under this Agreement, shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code. Rigel agrees during the term of this Agreement to create and maintain current copies or, if not amenable to copying, detailed descriptions or other appropriate embodiments, of all such intellectual property. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against Rigel under the Bankruptcy Code, Janssen shall be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, and the same, if not already in its possession, shall be promptly delivered to Janssen, upon written request therefor by Janssen, (a) upon any such commencement of a bankruptcy proceeding, unless Rigel elects to continue to perform all of its obligations under this Agreement, or (b) if not delivered under clause (a) above, upon the rejection of this Agreement by or on behalf of Rigel.

14.12 NO OTHER REPRESENTATIONS. Each of the Parties hereto acknowledges and agrees (a) that no representation or promise not expressly contained in this Agreement has been made by the other Party hereto or by any of its agents, employees, representatives or attorneys; (b) that this Agreement is not being entered into on the basis of, of in reliance on, any promise or representation, expressed or implied, covering the subject matter hereof, other than those which are set forth expressly in this Agreement; and (c) that each Party has had the opportunity to be represented by counsel of its own choice in this matter, including the negotiations which preceded the execution of this Agreement.

IN WITNESS WHEREOF, the Parties hereto have duly executed this Agreement.

RIGEL PHARMACEUTICALS, INC.	JANSSEN PHARMACEUTICA, N.V.
By: /s/ James M. Gower	By: /s/ Gustav van Reet
Name: Jim Gower	Name: Dr. Gustav van Reet
Title: President and CEO	Title: Managing Director
	By: /s/ Didier de Chaffoy de Courcelles
	Name: Didier de Chaffoy de Courcelles
	Title: Vice President Biological Research

EXHIBIT A

RESEARCH PLAN

SYNOPSIS

RIGEL-JANSSEN COLLABORATION PROPOSAL

APPROACH: To identify targets that regulate cell cycle checkpoint control mechanisms. This will be accomplished by introducing into selected tumor cells using proprietary retroviral delivery-vectors cDNA libraries and constrained 18mer random peptide libraries in order to alter the cellular phenotype of specific tumor cells. Using this approach in tumor cells, which exhibit uncontrolled proliferation, target-peptide pairs will be identified which restore normal cell-cycle progression and sensitivity to chemotherapeutic agents.

cDNA LIBRARIES: Human fetal liver and brain. The reason for choosing these tissues is that cells in these organs have a high degree on "differentiation control mechanisms" and hence should contain targets that are important in regulating the cell cycle.

PEPTIDE LIBRARIES: The first library to be tested will be a constrained 18mer random peptide library. Other libraries will be screened as necessary.

CELL LINES FOR PRIMARY SCREENS: Cell lines derived from Colon, Lung and Breast tumors will be studied. From Colon, the line HT-29; Lung, the cell lines A549 (p53 wt) and H-1299; and Breast, the line MDA-MB-231. For each cell line the p53, Rb, p16 and p21 status will be evaluated using antibodies and sequencing of the gene to determine the presence and absence of specific mutations. These will be compared to control levels from normal tissues.

PRIMARY SCREENS: For each of the above tumor cell lines, retrovirally delivered libraries (cDNA and random constrained peptide) will be introduced into cells. The cells will be stained with the Cell Tracker dye and monitored for cell division by high through put FACS. Cells that don't divide will be sorted and stained with a DNA labeling dye in order to identify those cells in G0/G1, S or G2M. After several rounds of enrichment, library members that block/arrest cell division in a particular phase of the cell cycle, will be identified.

SECONDARY SCREENS: Individual cDNA and peptide hits from the primary screens will be evaluated in the same FACS assay as above, and in proliferation and apoptosis assays in a "panel" of cell lines to be determined by the RMC.

PATHWAY MAPPING. Using the Yeast Two-Hybrid (YTH) technology cDNA hits (those found by Rigel in their functional screens, or by Janssen, such as Hrad17, Hrad1, etc.) will be used in YTH to find their interacting protein partners, and these will be evaluated in the above assays for function. Proteins that are demonstrated to significantly alter cell cycle in tumor cells, will be subjected to a YTH screen with a constrained peptide library

to find an enriched "peptide binding" library that can identify functional sites on these proteins in the above assays. The goal is to identify peptide-protein pairs that restore normal cell cycle responses in a significant number of tumor cell lines.

RESOURCES: 10 Rigel FTEs for 36 months.

IDENTIFICATION OF FUNCTIONAL PEPTIDE-TARGET INTERACTIONS REGULATING CELL CYCLE IN SPECIFIC TUMOR CELLS

JANSSEN PROJECT OUTLINE

INTRODUCTION

The hallmark of a malignant cell is uncontrolled proliferation. This phenotype is acquired through the accumulation of gene mutations, the majority of which promote passage through the cell cycle. Cancer cells ignore growth regulatory signals and remain committed to cell division. Classic oncogenes, such as RAS, lead to inappropriate transition from G1 to S phase of the cell cycle, mimicking proliferative extracellular signals. Cell cycle checkpoint controls ensure faithful replication and segregation of the genome. The loss of cell cycle checkpoint control results in genomic instability, greatly accelerating the accumulation of mutations which drive malignant transformation. Hence, checkpoint regulators, such as p53 and ATM (ataxia telangiectasia mutated), also function as tumor suppressors. Thus, modulating cell cycle checkpoint pathways with therapeutic agents could exploit the differences between normal and tumor cells, both improving the selectivity of radio- and chemotherapy, and leading to novel cancer treatments. THE GOAL OF THIS PROPOSAL IS TO IDENTIFY PEPTIDE/PROTEIN INTERACTIONS THAT INHIBIT THE ABILITY OF SPECIFIC TUMOR CELLS TO PROLIFERATE, BY ALTERING THEIR CAPACITY TO TRANSIT THROUGH VARIOUS STAGES OF THE CELL CYCLE. This will be accomplished by identifying intracellular targets, and their cognate regulating peptides, capable of inhibiting tumor cell progression through the cell cycle, either by activating cell cycle checkpoint pathways or ameliorating checkpoint defects (see Table 1 for summary). The identification of these targets will allow for low molecular weight compound screening to isolate activators or inhibitors of cell cycle checkpoint pathways.

Table 1 Summary of screens to identify functional peptide-target interactions regulating cell cycle in specific tumor cells.

SCREENING APPROACH	READOUT	LIBRARY STRUCTURE + TARGETING MOTIF
1. Functional screening with peptide libraries for inhibitors of tumor cell progression through various phases of the cell cycle	Identify tumor cells arrested in specific cell cycle phase using four-parameter cell-based high throughput FACS assay	- Linear 20 mer +/- NLS* - Constrained 18-mer stem loop +/- NLS - 4 helix bundle +/- NLS
2. Functional analysis of proteins (Hrad17, Hrad1, Hrad9, etc.) isolated by Janssen implicated in cell-cycle control.	Examine effect of protein, antisense, mutated protein or peptide binding library on tumor cells in assays under Specific Aim 1	
2.1 Retroviral-mediated functional analysis of cell cycle control proteins		- N/A
2.2 Large scale randon-mutagenesis analysis of cell cycle control proteins: Generation of libraries of mutant proteins		- Library of mutated proteins
2.3 Cell cycle control protein-binding peptide library screen (see 3.2)		- "enriched by binding" library: constrained 18 mer stem-loop +/- NLS
3. Elucidation of the signaling pathways that mediate the control of cell cycle checkpoints in specific tumor cells		-
3.1 Two hybrid screening of peptide hits from 1 to identify functional peptide-target protein pairs	LacZ+, His+	- cDNA library: - a specific tumor cells - a human fetal liver/brain

3.2 Isolation of peptides that bind to specific proteins implicated in cell cycle regulation and determination of their ability to specially inhibit tumor replication and progression through various phases of the cell cycle.	LacZ+, His+	-	"enriched by binding" peptide library: constrained 18 mer stem-loop +/- NLS
3.3 Cell cycle checkpoint pathway mapping	LacZ+, His+	-	cDNA libraries "enriched by binding" peptide library: constrained 18mer stem-loop +/- NLS

</TABLE>
* NLS = nuclear localization sequence

A. SPECIFIC AIMS

The outline of the Specific Aims below, is followed by a more detailed discussion of the Experimental Methods and the Design of the Project.

SPECIFIC AIM 1:

FUNCTIONAL SCREENING WITH PEPTIDE LIBRARIES FOR INHIBITORS OF TUMOR CELL PROGRESSION THROUGH VARIOUS PHASES OF THE CELL CYCLE.

Screens in specific aim 1 will be conducted on a panel of tumor cell lines to be chosen by Janssen. These cell lines will be selected based on their representation of important oncology markets, biological significance, and clinical relevance. The characteristics of the tumor cell lines are detailed in an addendum to be provided by Janssen. A Rigel-Janssen joint research committee will review this information to ensure that it includes information relating to culture conditions and molecular defects in key intracellular targets that could influence the assay conditions (e.g. p53, Rb status, etc.).

Tumor cells selected by Janssen will each be infected with three structurally different retroviral peptide libraries with and without sub-cellular localization sequences (Appendix A). These peptide libraries will consist of a linear 20mer with and without a nuclear localization signal (NLS), a stem loop constrained 18mer with and without an NLS, and a third constrained library containing a different scaffolding, such as a 4-helix bundle with and without an NLS. Library infected tumor cells which are inhibited in their progression through specific phases of the cell cycle will be selected using a high throughput fluorescent activated cell sorter (FACS) (Appendix B). After several rounds of enrichment, individual peptide sequences will be tested for inhibitory function. Validated peptide hits will be subjected to secondary assays in a broader panel of representative tumor cell lines to be chosen by Janssen in order to determine their physiologic characteristics and specificity. Peptides that demonstrate desirable characteristics will be used as bait in a yeast two-hybrid screen to locate their intracellular binding partners (see specific aim 3.1 for details). The right-hand side of Figure 1 illustrates this identification cycle for functional peptide-target protein interactions (the left-hand side will be discussed in section 2.3 and 3.3 below).

[Diagram]
(Figure 1)

SPECIFIC AIM 2:

FUNCTIONAL ANALYSIS OF PROTEINS IMPLICATED IN CELL CYCLE CHECKPOINT CONTROL.

Cell cycle checkpoint control proteins, selected by Janssen scientists, will be subjected to a detailed functional analysis to establish their potential as targets for further pharmaceutical development. Initial examples will include, but are not limited to, Hrad1 and Hrad17, two human homologues of S. POMBE proteins implicated in DNA damage-dependent and DNA replication-dependent cell cycle checkpoints. The genes encoding these proteins will be transduced into selected cell lines and analyzed for cell cycle perturbances. Mutagenesis studies will be conducted on each gene to identify mutants with dominant-negative effects on cell cycle

progression and checkpoint responses to anticancer agents. Together this information will provide insight into the role these proteins play in mammalian checkpoint control and how mutations in these genes may contribute to tumorigenesis and chemotherapeutic sensitivity. These cell cycle control proteins will be screened for interacting peptides in a yeast two-hybrid system. The binding peptides will be assayed for their ability to influence tumor cell growth and sensitivity to chemotherapic treatments.

2.1 Retroviral-Mediated Functional Analysis Of Cell Cycle Control Proteins.

Cell cycle control genes selected by Janssen will be cloned into Rigel's proprietary retroviral expression system for stable transduction into selected tumor lines. Optimized infection protocols will be developed for each cell line. Transduced cells will be analyzed for cell cycle effects and changes in apoptotic responses (by FACS-based ways described in Appendix B). The radiation and chemotherapeutic sensitivity of cells expressing these cell cycle control genes will be assayed in collaboration with Janssen scientists. Anti-sense versions of each gene will be assessed for loss-of-function phenotype and/or dominant negative effects in cell cycle assays.

2.2 LARGE-SCALE RANDOM-MUTAGENESIS ANALYSIS OF CELL CYCLE CONTROL PROTEINS: GENERATION OF LIBRARIES OF MUTANT PROTEINS.

Selected cell cycle control proteins will be randomly mutagenized to create libraries of mutated proteins (Appendix C) and screened for dominant negative cell cycle effects in different cell lines as described in Specific Aim 2.1.

2.3 CELL CYCLE CONTROL PROTEIN-BINDING PEPTIDE LIBRARY SCREEN.

The cell cycle control proteins defined above will be screened in a yeast two-hybrid assay for interacting binding peptides (as described in Specific Aim 3.2). These interacting peptides will be introduced into selected tumor cell lines to assess effects on cell cycle and sensitivity to chemotherapeutic treatments as described in Specific Aim 1.

SPECIFIC AIM 3:

ELUCIDATION OF THE SIGNALING PATHWAYS THAT MEDIATE THE CONTROL OF CELL CYCLE CHECKPOINTS IN SPECIFIC TUMOR CELLS

Specific aim 3 represents the final phase in the derivation of functional-based peptide-protein pairs that are members of a pathway(s) that regulate cell cycle in specific tumor cells.

3.1 TWO-HYBRID SCREENING OF PEPTIDE HITS TO IDENTIFY FUNCTIONAL PEPTIDE-TARGET PROTEIN PAIRS.

The peptide hits identified in Specific Aim 1 will be used as bait in a two-hybrid screen to identify their intracellular binding partners (Appendix D). This will identify peptide-target pairs that can be further assessed in secondary and orthogonal assays to be determined by the Rigel-

Janssen joint research committee for their potential to specifically inhibit tumor cells progression through various phases of the cell cycle. These protein targets will also be subjected to additional two-hybrid screening to identify neighboring interacting proteins that may also regulate the cell cycle and proliferation of tumor cells (see 3.3 below).

3.2 ISOLATION OF PEPTIDES THAT BIND TO SPECIFIC PROTEINS IMPLICATED IN CELL CYCLE REGULATION AND DETERMINATION OF THEIR ABILITY TO SPECIFICALLY INHIBIT TUMOR REPLICATION AND PROGRESSION THROUGH VARIOUS PHASES OF THE CELL CYCLE.

The cell cycle control proteins selected by Janssen (see Specific Aim 2.1) will be subjected to a two-hybrid screen using a combinatorial peptide library to identify specific binding peptides (Appendix E). The two-hybrid peptide libraries contain the same peptide structures and sub-cellular localization sequences as described in Specific Aim 1 and Appendix A. The isolated target-binding peptides will be assessed for their ability to inhibit cell cycle progression in tumor cells. Validated peptide hits will be subjected to secondary assays to confirm their function and specificity.

3.3 CELL CYCLE CHECKPOINT PATHWAY MAPPING.

The protein targets identified above (Specific Aim 2 and 3.1) will be screened for additional interactions with other proteins by yeast two-hybrid technology (Appendix D). These binding proteins will be assayed for their ability to halt tumor cell progression through various cell cycle phases. Those that have function in this basic assay will be subjected to a two-hybrid screen using a combinatorial peptide library to identify specific binding peptides (Appendix F). The two-hybrid peptide libraries contain the same peptide structures and sub-cellular localization sequences as described in Specific Aim 1 and Appendix A. The isolated target-binding peptides will be assessed for their ability to inhibit cell cycle progression in tumor cells. Validated peptide hits will be subjected to secondary assays to confirm their function and specificity. This process represents a reverse of what was described earlier in Specific Aim 1 and is illustrated in the left-hand side of Figure 1.

B. EXPERIMENTAL DESIGN AND METHODS

SPECIFIC AIM 1:

FUNCTIONAL SCREENING WITH PEPTIDE LIBRARIES FOR INHIBITORS OF TUMOR CELL PROGRESSION THROUGH VARIOUS PHASES OF THE CELL CYCLE.

RATIONALE:

Altered regulation of proteins that control cell cycle checkpoints may result in chromosomal instability which underlies the transformed state of many tumor cells. Using Rigel's high throughput genetic screens, it is expected that novel tumor-specific targets will be identified, which when bound to a peptide, will result in the cell being blocked from exiting a specific phase of the cell cycle.

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Rigel has demonstrated that it can identify and express cell cycle regulating proteins, and specific peptides derived from them, which arrest cells in a specific phase of the cell cycle (Appendix F). Consequently, it is expected that the use of combinatorial constrained peptide libraries delivered using a retroviral-based system will identify peptide families which interact with novel cell-cycle checkpoint regulating targets.

1.0 PEPTIDE LIBRARY SCREENING AND TARGET IDENTIFICATION USING A CELL CYCLE CHECKPOINT ASSAY.

Tumor cells selected by Janssen will be infected with each Rigel peptide library (Appendix A). The screening protocol and timeline for identification of the peptide inhibitors and their target proteins is shown diagrammatically in Figure 2 for each of the three structurally different peptide libraries.

(Figure 2)

Each of these peptide libraries will be packaged into infectious viral particles (for protocol, see Appendix G). Each library will be a mixture of random peptide sequences with and without a nuclear localization sequence (NLS) upstream of a reporter gene to identify infected cells and relative peptide expression (Appendix H). In fact, we have developed several retroviral constructs to control all aspects of peptide expression and localization. This gives us great flexibility when designing retroviral libraries within any cell line and with whichever characteristics are deemed necessary for intracellular peptide expression (Appendix I). The three structurally different peptide libraries will consist of a linear 20-mer (first year), a constrained stem-loop 18-mer (first to second year) and a third structure such as a 4-helix bundle to be determined by year three (Appendix A).

Each screen will start with production of the primary retrovirus peptide library. This primary library will be used to infect at least 10E9 tumor cells. After infection, the tumor cells will be loaded with a fluorescent dye (celltracker) that is uniformly partitioned into dividing cells. As cell division progresses, the fluorescence is diminished proportionately to the number of cell divisions. Hence, cells that fail to divide remain maximally bright (Appendix B). The screen is conducted over a time period such that, in tumor cells where no library is expressed, greater than 99% of the tumor cells undergo a sufficient number of cell divisions resulting in less than 1% of cells with the maximal celltracker fluorescence in the FACS. Prior to the high throughput FACS sort, cultures of cells are labeled with a DNA staining dye, such as Hoechst 33342, which enables the identification of viable cells in different phases of the cell cycle. Cells which are maximally bright with the celltracker dye (i.e. cells where the expressed peptide inhibits division) will be sorted according to the specific phase of the cell cycle in which they have been arrested (Appendix B). A positive control construct encoding the cyclin-CDK-inhibitor (CKI)-family member, p21, will be used to optimize the assay conditions in selected target cell lines. Enriched non-dividing tumor cell populations will be subjected to RT-PCR to amplify the integrated peptide sequences. The PCR material will be used to construct a new "enriched" retrovirus peptide library to initiate the next screening round.

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It will take approximately 5-7 rounds of enrichment to identify individual peptide sequences capable of inhibiting tumor cell cycle progression. For a discussion of the statistics associated with enrichment, see Appendix J. The most important factor that influences the number of enrichment rounds necessary to identify individual peptide hits is the ratio between real positive peptide hits in the original library and heritable false positives. The frequency of real positive peptide hits is dependent upon the qualitative ability of the peptide to access and, in the correct conformation, bind to the regulatory domains on proteins in the pathway of interest. This is why we use multiple scaffolding structures for presentation of random peptide surfaces and also different localization sequences fused to those peptide structures (Appendix A). Enrichment of real positive peptides becomes less efficient with false positive

rates above 2%. Consequently, great effort is placed in developing robust assays with multiple parameters being analyzed for a given biologic process.

Uneven RT-PCR amplification may decrease overall amplification of real peptides hits from one round to another. This is overcome by additional rounds of library enrichment and is why RT-PCR amplification is carefully monitored after each round of screening. We are also developing a direct biological rescue to expedite enrichment and to overcome any decrease in amplification of peptide hits due to uneven RT-PCR. Biological rescue involves direct transfer of recombinant retroviral inserts from positively identified cell clones into naive cells for retesting. By supplying retrovirus proteins GAG-POL-ENV to cells, integrated proviral transcripts encoding putative peptide hits are selectively re-packaged and secreted as new virions capable of infecting new cells. Positive cells can be converted to retroviral producers by superinfection of GAG-POL-ENV genes or alternatively, tetracycline-inducible packaging functions can be preengineered into target cell lines. By either strategy, peptides from enriched cells can be selectively transferred to new cells and re-tested for phenotypic effects, eliminating the time-intensive and potentially biased intermediary molecular cloning steps.

A separate strategy to enhance enrichment will involve a retroviral system with inducible expression (e.g. tetracycline dependent). Inducible transcription units can be placed within the retroviral vector; alternatively, inducible promoter elements may be inserted into the retroviral promoter within the LTR (see Appendix H). In this scheme, peptide expression is repressed following sorting to alleviate the peptide-specific cell cycle arrest and to allow a post-sort growout: Cells arrested due to non-peptide specific causes, such as mutation or aneuploidy, would remain arrested. Re-induction of the peptide expression will reinstate the arrested phenotype in true peptide hits, which can subsequently be enriched in another round of sorting.

Once enrichment is achieved and individual peptide sequences are shown to effect inhibition in an independent assay, the peptides will. be introduced into a panel of tumor cells (to be obtained from the NCI) for secondary and orthogonal assays as determined by the Rigel-Janssen joint research committee. Validated peptides will then be used as bait to isolate their interacting protein targets by two-hybrid approaches (see section 3 for details).

SPECIFIC AIM 2:

FUNCTIONAL ANALYSIS OF PROTEINS IMPLICATED IN CELL CYCLE CHECKPOINT CONTROL.

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RATIONALE:

Cell cycle control genes identified by Janssen, including (but not limited to) human homologues of S. POMBE RAD1+ and RAD17+ checkpoint genes, will be expressed in selected cell lines for detailed functional analysis to establish their potential as targets for further pharmaceutical development. Expression of dominant-negative mutants of cell cycle checkpoint regulators, such as p53 and hBUB1. account for some inappropriate tumor cell responses to DNA damaging and spindle-disrupting agents, respectively. Hence, mutagenesis studies will be conducted on each cell cycle control gene to identify dominant-negative mutants of these proteins. This will serve to map functional domains important in the regulation of cell cycle checkpoint function and chemotherapeutic sensitivity. Selected cell cycle control proteins will be screened for interacting peptides in a yeast two-hybrid system. These binding peptides will be assayed for their ability to influence tumor cell growth and for their sensitivity to chemotherapeutic treatments.

2.1 RETROVIRAL-MEDIATED FUNCTIONAL ANALYSIS OF CELL CYCLE CONTROL PROTEINS.

Cell cycle control genes selected by Janssen will be transferred into Rigel's retroviral system for stable expression and functional analysis in selected tumor cell lines. Encoding sequences will be cloned into the multiple cloning region of the basic retroviral vector construct (Appendix H). An internal ribosome entry site (IRES), placed immediately 3' of the multiple cloning site, drives cap-independent translation of downstream encoding sequences. This allows co-translational selection with a downstream FACS-selectable marker (e.g. GFP). Infectious retroviral particles are produced by transient transfection of retroviral vector constructs into high efficiency packaging cell lines (Appendix G), harvested, and used to infect target cell lines for stable integration into the target cell genome. Optimal infection protocols will be developed for each cell line using a GFP control vector. A generic protocol is detailed in Appendix G. Examples of infection rate for various tumor cell lines is shown in Table 2.

TABLE 2. INFECTION RATES WITH RIGEL RETROVIRAL CONSTRUCTS FOR VARIOUS TUMOR CELL LINES.

<TABLE>
<CAPTION>
- ----------

CELL LINE	INFECTION EFFICIENCY (%)
<S>	<C>
A549 (non-small cell lung cancer)	>80
HeLa (cervical carcinoma)	>70
T47D (breast cancer)	>70
SW480 (colorectal cancer)	>70
CEM (T-lymphoblastoid leukemia)	>30

</TABLE>

In most cases, transduction rates of >70% are achievable with limited optimization of the standard protocol. Occasionally, cells express low levels of the retroviral receptor recognized by the retroviral envelope protein. This may be compensated by engineering the target cell lines to express higher receptor levels by introducing the ecotropic envelope protein receptor (EcoR), a basic amino acid transporter. For example, infection efficiency of Jurkat T-lymphoblastoid

leukemia cells was enhanced from ~15% to >90% in EcoR-expressing lines. Alternatively, retroviral vector particles may be pseudotyped with the Vesticular Stomatitis Virus G-protein (VSV-G), which interacts with membrane lipids (phosphatidylserine) to promote fusion.

The infection efficiency of individual constructs is monitored via IRES-driven GFP co-expression by FACS and/or microscopy. Cells expressing cell cycle control genes will be analyzed for direct cell cycle effects and induction of apoptosis (Annexin-V binding) by FACS-assay. Furthermore, the transduced cells will be assayed for chemotherapeutic (e.g. DNA replication inhibitors, anti-metabolites, microtubule-disrupting agents) and radiation (UV and gamma) sensitivity alterations in collaboration with Janssen scientists.

Anti-sense versions of each cell cycle control gene will be constructed by inserting the cDNA sequence in reverse orientation into the basic vector. The insert length will be varied, creating small libraries of specific anti-sense effectors for each gene. These constructs will be used to generate infectious retroviral vector particles and transduced into selected cell lines as described above. The transduced cells will be assayed for loss-of-function and/or dominant negative effects on cell cycle checkpoint control as described above.

2.2 LARGE SCALE RANDOM-MUTAGENESIS ANALYSIS OF CELL CYCLE CONTROL PROTEINS: GENERATION OF LIBRARIES OF MUTANT PROTEINS.

The polymerase chain reaction (PCR) can be used to generate comprehensive, unbiased single-point mutation libraries. Essentially, the mutagenesis strategy takes advantage of the ability of Taq DNA polymerase to alter the fidelity of replication by doping the PCR reaction with divalent cations. The use of magnesium to stabilize non-complementary base-pairs and manganese to impair recognition of complementary base-pairs allows mutation of up to 2% of all nucleotides per gene. The mutation frequency can be controlled by titrating levels of the divalent cations to produce an average of one mutation per gene. The use of altered dNTP ratios can eliminate the inherent bias for transition-mutations in PCR mutagenesis. This controlled PCR mutagenesis procedure can create complex, representative, mutant cDNA libraries for genes of any length which can then be used to probe for critical functional domains of the encoded protein. These libraries are screened in the functional assay detailed in Appendix B. The Janssen-Rigel joint research committee will determine treatment regimes with relevant DNA damaging agents, radiation or chemotherapeutics for the tumor cells expressing different cell cycle control gene mutant libraries.

2.3 CELL CYCLE CONTROL PROTEIN-BINDING PEPTIDE LIBRARY SCREEN.

The cell cycle control proteins defined above will be screened in a yeast two-hybrid assay for interacting peptides as described in Specific Aim 3.2. Interacting peptide encoding sequences will be transferred into a shuttle vector for transfer into tumor cell lines. Peptide effects on cell cycle checkpoint function will be assayed as described in Specific Aim 2.1.

SPECIFIC AIM 3:

ELUCIDATION OF THE SIGNALING PATHWAYS THAT MEDIATE THE CONTROL OF CELL CYCLE CHECKPOINTS IN SPECIFIC TUMOR CELLS

RATIONALE:

Peptides that inhibit the ability of tumor cells to transit through specific phases of the cell cycle do so by binding to intracellular proteins

that are members of pathways which control cell replication. Identification of functional peptide-target protein pairs which significantly alter these responses will enable screening for low molecular weight inhibitory compounds.

3.1 TWO-HYBRID SCREENING OF PEPTIDE HITS TO IDENTIFY FUNCTIONAL PEPTIDE-TARGET PROTEIN PAIRS.

The peptide hits identified in specific aim 1 will be used as bait in a two-hybrid screen to identify their intracellular binding partners. This will identify peptide-target pairs that can be assessed in secondary and orthogonal assays for their potential to specifically inhibit tumor cell transition through the cell cycle and proliferation. The cDNA libraries to be used are derived from the specific tumor cells used in the screen, and from a control library derived from human fetal liver and brain.

The identified peptide/protein pairs will be assessed for their ability to regulate tumor cell growth and cell cycle progression in a panel of tumor cell lines derived from a variety of sources (e.g. National Cancer Institute tissue bank) in order to determine specificity, in addition to being examined for their effect on normal cells, such as human epithelial and endothelial cells and murine primary bone marrow cells. These protein targets will also be subjected to additional two-hybrid screening to identify neighboring interacting proteins (pathway mapping) involved in cell cycle pathways in tumor cells (see section 3.3).

The screening protocol for identification of peptide binding proteins is summarized in Appendix E. The methods are as follows: oligo sequences encoding the peptide hits will be cloned into pAS2-1K to fuse to the C-terminal of GAL4 DNA binding domain. The oligos can also be cloned into pAS2N to fuse to the N-terminal of GAL4 DNA binding domain. Both bait plasmids can be used for subsequent screenings.

The bait plasmids will be transformed into the Y190 yeast strain. This yeast strain has the highest sensitivity for yeast two-hybrid screening. Optimal 3AT concentration needed to suppress any HIS background expression will be determined on SD-WH+3AT plates.

cDNA libraries from both tumor cells and fetal and human brain will be used to transform the yeast already containing the bait plasmid. At least 20 million transformants from each library will be screened on SD-LWH+3AT plates. HIS+ and LacZ+ clones will be grown up in SD-L liquid medium to retrieve plasmid and for retransformation into Y190 to verify the binding specificity.

3.2 ISOLATION OF PEPTIDES THAT BIND TO SPECIFIC PROTEINS IMPLICATED IN CELL CYCLE REGULATION AND DETERMINATION OF THEIR ABILITY TO SPECIFICALLY INHIBIT TUMOR REPLICATION AND PROGRESSION THROUGH VARIOUS PHASES OF THE CELL CYCLE.

Hrad1, Hrad17, and other proteins implicated in regulating the cell cycle identified by Janssen (see Specific Aim 2), will be subjected to a yeast two-hybrid screen using a peptide library to identify binding peptides as described in Appendix F. The identified binding peptides will then be assessed for their ability to inhibit specific tumor cells in their progression through the cell cycle. Validated peptide hits will be subjected to secondary assays to confirm their function and specificity. This will identify functional peptides that bind to the cell cycle control proteins and inhibit tumor growth (left side of Figure 1).

3.3 CELL CYCLE CHECKPOINT PATHWAY MAPPING.

The second-level two-hybrid screening of protein targets that bind to peptide hits (from Specific Aim 3.1), or cell cycle control proteins selected by Janssen (Specific Aim 2.1). is referred to as functional-based pathway mapping. This will elucidate interacting members within the cell cycle checkpoint control pathway. These interacting proteins will be assayed for their ability to modulate growth and progression through the cell cycle in "normal" and tumor cell lines. Those with function will be subjected to a two-hybrid screen using a peptide library to identify binding peptides (Appendix F). The protocol is the same as described in Appendix E, except that peptide libraries are used instead of cDNA libraries. These binding peptides will then be assessed for their ability to inhibit growth and cell cycle progression in tumor cells. Individual peptide hits will be subjected to secondary assays to confirm their function and specificity. This will produce additional peptide/protein pairs capable of regulating tumor growth.

C. INITIAL STEPS FOR TARGET IDENTIFICATION/VALIDATION (SEE FLOWCHART IN APPENDIX K)

It is important to recognize that once a protein target has been identified that binds to a confirmed peptide hit, by virtue of the functional screen that produced the peptide hit the functional relationship of the target protein to the pathway of interest is defined for that particular cell type. False positives only arise if the peptide hit binds to additional proteins not related

to the functional pathway altered by the peptide hit. Below is a protocol to discriminate false positives from pathway specific peptide/protein target pairs.

Once the desired change in the phenotype of the library-infected cells is achieved, the peptides responsible will be sequenced. Individual peptide sequences derived from the libraries will be tested for their ability to inhibit tumor cell progression through various phases of the cell cycle in the original screening assay under Section 1.0. Individual peptides, with inhibitory effects will be subjected to two-hybrid screening using cDNA libraries derived from human tumor cell lines. cDNAs that are isolated from the two-hybrid screen and retested for binding to the peptide will be defined as initial targets. In parallel with the two-hybrid screening, peptide hits will be subjected to secondary screens to test their specificity in several tumor cell lines (see

Appendix K). Orthogonal assays will include evaluating peptide effects on the cell cycle and proliferative characteristics of normal and primary cells.

Once protein targets that bind to the functional peptides have been isolated and confirmed by two-hybrid screening, their ability to interact in mammalian cells will be assessed. This will be accomplished by uniquely tagging both the target protein and peptide and then immunoprecipitating in either direction to determine if its partner can be co-immunoprecipitated. After this test, the resulting peptide/protein pairs can be subjected to numerous secondary and orthogonal assays to confirm their role in cell cycle regulation. The type of peptide/protein pairs identified will dicate the exact assays performed. These assays include over-expression of the target protein and dominant negative mutants, anti-sense expression of the target protein sequence, complementation by over-expressing the target protein in cells expressing the inhibitory binding peptide, and knockout somatic cell lines of the target protein. These assays will assist in the determination of targets to be introduced into Janssen small molecule compound screens. Below is a brief description of the rationale and approach for each of the assays described above.

Over-expression of the target protein may modulate cell cycle progression or modify checkpoint responses in tumor cells, thereby implicating a regulatory role. This can be accomplished very simply with Rigel's retroviral vector system. By using reporter genes downstream of the cDNA encoding the target protein we can track infected cells and determine the relative concentration of the target protein. This will allow us to titrate its biological effect as a means to confirm the target protein's role in inhibiting tumor cell progression through the cell cycle. If overexpression of the protein target influences the cell cycle, mutant libraries of the protein can be screened for loss-of-function as described below.

Target proteins will be randomly mutated (see Appendix C) and screened in FACS assay (Appendix B) for mutant proteins that inhibit tumor cell cycle function. Two variations of this approach allow us to narrow our screen of mutant target proteins. One variation is to perform mutagenesis on the target cDNA and then subject them to a 2-hybrid screen with the cognate peptide as bait to identify mutants that no longer bind the peptide. These mutant proteins can be tested for loss-of-function in mammalian cells. Alternatively, the peptide is chemically crosslinked to the target protein to identify the region bound by the peptide using mass spectrometry. Then the peptide-binding region of the target protein is randomly mutated and the clones screened for their ability to inhibit tumor cell growth. The advantage of this variation is that the regulatory domain of the target protein is identified.

A third approach to confirming the role of the target protein in tumor cell cycle regulation is complementation. The screening cell lines are infected with the peptide and its target protein that is under the control of an inducible promoter such as tetracycline or metallothionein. The target protein is induced and tested for its ability to overcome the inhibition of the peptide.

Finally, somatic and germline knockout cell lines of the target protein can be generated to assess tumor cell growth in the absence of the target protein. Although this approach takes

longer, in the case of the germline knockout mice they allow for in vivo experiments to assess the function of the target protein.

Some or all of the above methods can be employed to confirm that a peptide/protein pair, identified in the initial screen, functions. It will be the task of the joint scientific board from Rigel and Janssen to determine which assays are necessary to sufficiently define a functional peptide/ protein pair for the next phase of development, specifically small molecular weight compound screening.

D. HEADCOUNT

To run optimally, the project will take 10 Rigel FTEs:

XIANG XU: Dr. Xu is the Project leader for the Cell Cycle Regulation Project. She will coordinate all scientific and administrative aspects of the project. In addition, she will carry out functional analysis of specific targets identified in the screens and in the secondary two-hybrid analyses. She is full time on this project.

JIM LORENS: Dr. Lorens is Head of Technology Development at Rigel. He will work directly on retroviral vector design and library rescue techniques, in addition to carrying out many of the experiments detailed under Specific Aim 2, which is the analysis of proteins identified by Janssen that regulate cell cycle checkpoint controls. He is full time on this project.

YNGJU JANG: Y. Jang is a Senior Research Associate who is responsible for conducting the cell based high throughput screens on the different tumor cell lines. She will carry out the primary infections with the libraries on the different tumor cells and do the different labeling steps to prepare the cell lines for HTS. She will also help in the library rescue and re-infection steps. She is full time on this project.

YASUMICHI HITOSHI: Dr. Hitoshi is a Senior Scientist responsible for carrying out functional analysis of specific targets identified in the HTS assays. In addition, he will carry out the generation of the "protein mutant libraries" of specific proteins identified by Janssen and characterize the functionally important mutants. He is full time on this project.

DAVID PADILLA: D. Padilla is a cell biology Research Associate responsible for all the tissue culture work for the project. He maintains all the different tumor cell lines, the Phoenix packaging cell line, and the sorted cell populations. He is full time on the project.

RANDY ARMSTRONG: R. Armstrong is the Senior Research Associate in charge of retroviral library design and production. He is responsible for the generation of all peptide libraries with their various scaffolds and localization sequences. He will perform the library rescue for the peptide screens, the subsequent subcloning of both the peptide hits and the targets into shuttle vectors for post two-hybrid functional analysis. He is full time on this project.

BETTY HUANG: B. Huang is the Senior Research Associate in charge of two-hybrid screening. She is responsible for setting up and carrying out all the two-hybrid assays, analyzing and isolating full-length clones, and generating the cDNA libraries. She is full time on this project.

YING LUO: Dr. Luo is Head of Target Identification and the two-hybrid technology group at Rigel. He is responsible for developing and constructing the vectors, as well as analyzing the results of the screens. He will develop and maintain the database of genes derived from two hybrid technology and the supporting bioinformatics. He will also establish and implement mammalian two-hybrid screening. He is full time on this project.

JOHN PATTON: J. Patton is the Research Associate in charge of all the DNA sequencing. This includes sequencing of all rescued libraries (to check for enrichment and contamination), all verified peptide hits, and all two-hybrid hits. He is also responsible for managing the sequence database and all related DNA bioinformatics of the project. He will coordinate the data entry into the Cell Cycle database. He is full time on this project.

DENISE PEARSALL: D. Pearsall is a Senior Research Associate in charge of analyzing all the peptide hits in different tumor cell lines, determining peptide hit specificity, and conducting secondary proliferation assays in normal and transformed cell lines. She is also responsible for coordinating all the initial steps in the cell based high throughput screens. She is full time on this project.

BILL THRONDSET. B. Throndset is the Senior Research Associate in charge of the high-speed flow cytometry and is responsible for setting-up and implementing all the FACS-based assays. He win perform these assays and sort the library hits for the Cell Cycle project. He will also supervise the FACS-associated bioinformatics for all the screens. He is full time on this project.

JEFF QUAST: J. Quast is a molecular biology Research Associate in the target identification group. He is responsible for all the support work on the two-hybrid analyses, including media prep, plate pouring, minipreps, colony picking, gel analysis, and subcloning. He is full time on this project.

APPENDIX A

[diagram]

APPENDIX B

FUNCTIONAL SCREEN FOR PEPTIDE INHIBITORS OF TUMOR CELL PROGRESSION

[diagram]

APPENDIX C

MUTAGENIC PCR GENERATES A LIBRARY OF RANDOM TARGET CDNA VARIANTS

[diagram]

APPENDIX D

YEAST TWO-HYBRID SCREENING

[diagram]

1. GROW UP YEAST REPORTER STRAINS ON YPD PLATES FROM FROZEN STOCK.

Since no antibiotics are added into the yeast medium, very stringent sterilization procedures are required during inoculation.

There are many reporter strains available from different resources. In general, Y190 consistently showed higher sensitivity than other yeast strains such as HF7c. Yeast reporter strains with both a lacZ reporter gene and a HIS3 reporter gene are strongly recommended. HIS selection will ensure that only interacting clones will grow, which makes colony picking much easier later.

2. DETERMINE OPTIMAL 3AT CONCENTRATION.

3AT can be used to suppress background expression from the HIS reporter gene of Y190. 3AT concentration varies among different reporter strains and ranges from 0 mM (HF7c) to 15 mM (Y190). To test the optimal concentration of 3AT, one yeast colony should be re-suspended in 10 ml of TE. 100 micoliters of the re-suspended yeast is spread on SD-H+0mM3AT, SD-H+5mM3AT, SD-H+10mM3AT, SD-H+15mM3AT, SD-H+25mM3AT, and SD-H+40mM3AT plates. Although 15 mM 3AT is sufficient to suppress background HIS expression of Y190, higher concentrations of 3AT (30-40 mM) are routinely used in our cDNA library screening.

3. CONSTRUCT BAIT PLASMID.

pAS2/pACT2 series plasmids showed higher level of sensitivity than pGAD424 /pGBT9 series plasmids (Estojak et al 1995; Legrain et al. 1994). The disadvantage of using pAS2 is the large size of this plasmid (8 kb), which may present a challenge to cloning large cDNA fragments into the plasmid. Peptide fragments should fused to the C-terminal and/or N-terminal of GaL4 binding domain in frame (Figure 4A). The junction sequence between Gal4 and cDNA should have a GGG amino acid sequence to avoid any interruption of domain structure. Alternatively, a constrained peptide presentation structure may be used. Either full-length cDNA or partial fragments can be used to generate bait plasmid.

4. TRANSFORM BAIT INTO YEAST: 1ST ROUND.

1 ug of bait plasmid is transformed into Y190 with small-scale yeast transformation protocol. Transformants should be plated on SD-W, SD-WH, and SD-WH+3AT(5-40mM) plates. A LacZ color assay can also be done after colonies grow to a diameter of 1mm. If colonies grow up on SD-WH+40mM3AT plates after 3 days incubation and/or LacZ color assay of these colonies show a positive result after only 30 minutes incubation with X-Gal, the bait gene is not suitable for two-hybrid screening without further modification. The bait gene itself may be able to activate transcription of reporter genes HIS/lacZ.

Although co-transformation of the bait plasmid and cDNA library can be done in a single step, co-transformation efficiency is at least 10 fold lower than single plasmid transformation. A mating approach may also be used to introduce cDNA library into yeast cells containing the bait vector. Please refer to the protocol published by Finley and Brent (Finley and Brent, 1994).

5. TRANSFORM CDNA LIBRARY: 2ND ROUND.

Y 190 containing bait plasmid is grown up for second round of transformation by cDNA library plasmid. Incubation time after transformation varies significantly

from 4 days to 11 days.

6. IDENTIFY POSITIVE CLONES.

Identification of positive clones needs experience. It should also be pointed out that background colonies at lightly populated areas of the plates tend to grow bigger, occasionally reaching the size of a positive colony in a dense area on the same plate. The size of the positive colony should be at least 4 times bigger than the neighboring background colonies. Positive colonies may also turn red faster.

7. PERFORM LACZ COLOR ASSAY.

Positive colonies should be re-streaked to another SD-LWH+3AT plate to isolate single colonies for color assay and plasmid retrieval. If a colony does not turn blue after a 4-hour incubation, strong protein-protein interaction is highly unlikely. It is not recommended to pick positive clones after 12 hours incubation, except when the protein-protein interaction being studied is very weak.

8. RETRIEVE PLASMIDS.

There are several methods to retrieve plasmids from yeast, ranging from lyticase lysis to glass beads. Electroporation is by far the most efficient method to transform plasmids from yeast miniprep into E. COLI. Bait and cDNA plasmid may carry different antibiotic selection markers to facilitate separation in E. COLI. For example, Rigel's bait plasmid carries a Kan-TM gene and the cDNA plasmid carries an Amp-TM gene.

9. VERIFY POSITIVE CLONES.

cDNA clones recovered from positive HIS/lacZ double colonies should be re-transformed into yeast with other non-specific bait controls to rule out non-specific binding. IN VITRO protein binding assays and function assays should also be done to rule out false positive clones.

2

Yeast Two-Hybrid Screening

[diagram]

1

From Identified Gene to Peptide Hits

[diagram]

Appendix E

3

Appendix F

Retrovirally expressed cell cycle control proteins and peptides induce cell cycle arrest

DIAGRAM

DIAGRAM

DIAGRAM

4

Appendix G

Protocol for Transfection of Phoenix Cells and Infection of Nonadherent Target Cells

DIAGRAM

Day 1:

Seed Phoenix cells (Es or As) in 10cm plates at 5 x 10x6 cells in 6 ml (DMEM + 10% FBS + Pen/Strep) per plate the day before transfection.

Day 2:

Allow all reagents to reach room temperature 30 min. before starting. Add 50 microM chloroquine at 8 microliter/plate (50 microM final) before preparing the transfection solution.

Mix CaPO4 reagents in 15 ml polypropylene tube:

Per plate: 10 micrograms DNA
122 microliters 2M CaCl2
876 microliters H2O
1.0 ml 2X HBS

Add 2X HBS and depress the expulsion button completely to bubble air through the mix for 10 secs. Immediately add mixture gently dropwise to plate. Incubate 3-8 hours. Remove medium and replace with 6.0 ml DMEM-medium.

Day 3:

Change medium again to 6.0 mls of medium optimal for the cells to be infected. Move to 32 degree C either in the morning or afternoon depending on the Phoenix cell confluency and whether you will infect at 48 or 72 hrs after transfection.

Day 4 or 5:

Collect virus supernatant from transfected plates (6.0 ml) into 50 ml tubes and add protamine sulfate to a final concentration of 5 micrograms/ml. Pass through a 0.45 microm filter. Count target cells and distribute 10x7 cells per 10 cm plate transfected to 50 ml tubes and pellet 5 min. Resuspend each pellet of target cells in virus supernatant and transfer to a 6 well plate at 1.0-1.2 ml per well. Seal plate with parafilm and centrifuge at RT for 30-90 min. at 2500 RPM. Remove parafilm and incubate plate over night at 37 degrees C.

Day 5:

Collect and pellet each well of target cells. Resuspend in 3 ml medium and transfer back to the same 6 well plate. Infection can be repeated by refeeding the Phoenix cells with 6ml fresh medium and reinfecting the same cells again up to 3 times to increase % of cells infected (for instance at 48, 56, and 72 hours)

Day 7 or 8:

At 48 to 72 hrs. post infection, target cells are ready to analyze for expression.

APPENDIX H

[diagram]

APPENDIX I

RETROVIRAL LIBRARY DESIGN FEATURES

[diagram]

APPENDIX J

[chart]

APPENDIX K

FLOW CHART FOR FUNCTIONAL SCREENS

(IDENTIFICATION OF FUNCTIONAL PEPTIDE/PROTEIN PAIRS)

[diagram]

10

RIGEL - JANSSEN COLLABORATION

[chart]

11

TIMELINES FOR RIGEL SCREENS

[diagram]

12

RIGEL - JANSSEN COLLABORATION

IDENTIFICATION OF NOVEL DRUG DISCOVERY TARGETS

[diagram]

[diagram]

[diagram]

13

RIGEL - JANSSEN COLLABORATION

IDENTIFICATION OF NOVEL DRUG DISCOVERY TARGETS

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

14

RIGEL - JANSSEN COLLABORATION

IDENTIFICATION OF NOVEL DRUG DISCOVERY TARGETS

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

15

RIGEL - JANSSEN COLLABORATION

IDENTIFICATION OF NOVEL DRUG DISCOVERY TARGETS

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

16

RIGEL - JANSSEN COLLABORATION

[diagram]

[diagram]

17

RIGEL - JANSSEN COLLABORATION

[diagram]

[diagram]

[diagram]

[diagram]

[diagram]

18

RIGEL - JANSSEN COLLABORATION

[diagram]

[diagram]

[diagram]

EXHIBIT B

RIGEL TECHNOLOGY ASSAYS

EXHIBIT C

FORM OF INVOICE

[Rigel Letterhead]

INVOICE NO. [__]

[Invoice Date]
Janssen Pharmaceutica NV
F.A.O. Lidi Van Gool
Turnhoutseweg 30
2340 Beerse
Belgium
VAT number 403834160

COLLABORATION AGREEMENT BETWEEN RIGEL, INC. AND JANSSEN PHARMACEUTICA, N.V.
DATED DECEMBER 4, 1998

Dear Ms. Van Gool:

Pursuant to Section [ ] of the above agreement, please pay to Rigel the following amount for [description of services for research funding or a milestone event for milestone payments, or make reference to net sales report from Janssen for royalty payments]:

US$ [ ]

Please remit the above amount within fifteen (15) days from the date this invoice by wire transfer to the following account:

[account information]

Sincerely,

Rigel, Inc.

- ----------

EXHIBIT D

STANFORD AGREEMENTS

AGREEMENT

Effective as of October 7, 1996 ("Effective Date"), THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, a body having corporate powers under the laws of the State of California ("STANFORD") and RIGEL PHARMACEUTICALS, INC., a Delaware corporation having a principle place of business at 24 Windsor Drive, Hillsborough, CA 94010 ("RIGEL"), agree as follows:

1. BACKGROUND.

1.1 STANFORD has an assignment of U.S. Patent Application No. 08/589,109, entitled "Methods for Screening for Transdominant Effector Peptides and RNA Molecules" (the "NOLAN/ROTHENBERG PATENT APPLICATION") claiming an invention developed in the laboratory of Dr. Garry Nolan (the "Invention"), and any Licensed Patent(s), as hereinafter defined, which may claim such Invention.

1.2 STANFORD has certain biological materials and other know-how ("Know-How"), as herein defined, pertaining to the Invention.

1.3 STANFORD desires to have the Know-How and Invention perfected and marketed at the earliest possible time in order that products resulting therefrom may be available for public use and benefit.

1.4 RIGEL desires a license under said Know-How, Invention, and Licensed Patent(s) in the field of use of gene transfer technologies, including retrovirally mediated nucleic acid libraries, for drug development, drug delivery, drug screening, and target analysis and discovery associated with the development, manufacture, use and sale of Licensed product(s), as defined below.

1.5 RIGEL acknowledges that certain of the Cell Lines (as defined below) were made in the course of research supported by Progenesys.

1.6 The patent application entitled "Methods for Screening for Transdominant Intracellular Effector Peptides and RNA Molecules," which claims technology useful in the field and which was developed in the laboratory of Dr. Garry Nolan (the "Nolan Patent Application"), has previously been assigned to RIGEL.

2. DEFINITIONS.

2.1 "LICENSED BIOLOGICAL MATERIALS" means the materials listed on Exhibit A, including certain vector libraries ("Vector Libraries") and cell lines ("Cell Lines") set forth therein, as amended from time to time upon the parties' mutual written consent.

2.2 "LICENSED KNOW-HOW" means all know-how necessary or useful for the commercial exploitation of the Licensed Patents in the Licensed Field of Use, including without limitation all know-how, trade secrets, protocols, information, processes or other subject matter

which is either disclosed in the Nolan/Rothenberg Patent Application, or necessary or useful to practice the licenses granted to RIGEL in this Agreement with respect to the Invention. Licensed Know-How excludes the Licensed Patents and includes the Licensed Biological Materials.

2.3 "LICENSED PATENT(S)" means any Letters Patent, both foreign (subject to Section 7) and domestic, issued upon (i) the Nolan/Rothenberg Patent Application (STANFORD's U.S. Patent Application Serial Number 08/589,109, filed January 23, 1996), (ii) any substitutions, divisionals, continuations, and continuations-in-part (to the extent such continuations-in-part claim subject matter disclosed or claimed in the Nolan/Rothenberg Patent Application as filed on January 23, 1996 and to the extent that the practice of an invention claimed in a Licensed Patent issuing from a patent application other than such continuation-in-part would infringe a claim of Licensed Patent issuing from such continuation-in-part), and (iii) any foreign counterparts of (i) or (ii).

2.4 "LICENSED TECHNOLOGY" means the Licensed Patent(s) and the Licensed Know-How.

2.5 "LICENSED PRODUCT(S)" means:

(a) any product, the manufacture, use, sale, offer for sale or import of which:

(1) is covered by a valid claim of an issued, unexpired Licensed Patent(s) directed to the Invention (claim of an issued, unexpired Licensed Patent(s) shall be presumed to be valid unless and until it has been held to be invalid by a final judgment of a court of competent jurisdiction from which no appeal can be or is taken), or

(2) is covered by any claim being prosecuted in a pending application directed to the Invention, which claim has not been pending for more than three (3) years from first filing of such claim;

(b) any product which directly incorporates any of the Licensed Biological Materials; or

(c) any product which would not, but for the use of the Licensed Biological Materials, have been identified, discovered, or developed.

2.6 "NET SALES" means the gross revenue derived by RIGEL and/or RIGEL's sublicensee(s) from the sales of Licensed Product(s), less the following items insofar as they actually pertain to the disposition of such Licensed Product(s) by RIGEL or RIGEL's sublicensee(s), are included in such gross revenue, and are separately billed:

(a) Import, export, excise and sales taxes, and custom duties;

(b) Credit for returns, allowances, trades, or retroactive price adjustments;

(c) Transportation charges, issuances and allowances;

(d) Discounts actually allowed; or

(e) Royalties payable to third parties on the manufacture, use, sale, offer for sale or import of Licensed Products.

2.7 "LICENSED FIELD OF USE" means the use of gene transfer technologies, including retrovirally mediated nucleic acid libraries, for drug development, drug delivery, and target analysis and discovery. Solely with respect to the phiNX Cell Lines set forth on Exhibit A, the Licensed Field of Use excludes the use of such Cell Lines, derivatives or vectors thereof or other tangible products that are a direct lineal descendent from such Cell Lines (although obtained in any manner therefrom), wherein cells treated with any one or more of the aforementioned materials are contained within a human subject or are subsequently transplanted into a human subject.

2.8 "EXCLUSIVE" means that, subject to Article 4, STANFORD shall not grant further licenses in the Licensed Field of Use.

3. GRANT.

3.1 STANFORD hereby grants and RIGEL hereby accepts a worldwide license in the Licensed Field of Use under STANFORD's right, title and interest in the Licensed Patents and the Vector Libraries to make, use, sell, offer for sale and import Licensed Product(s).

3.2 The license granted in Section 3.1 is Exclusive, including the right to sublicense pursuant to Article 13, in the Licensed Field of Use for a term (the "Exclusivity Term") commencing as of the Effective Date and ending on the first to occur of the following:

(a) twenty (20) years from the Effective Date; or

(b) ten (10) years from the date of first commercial sale of a Licensed Product(s) by RIGEL or RIGEL's sublicensee(s). RIGEL agrees to promptly inform STANFORD in writing of the date of first commercial sale of Licensed Products. After expiration of the Exclusivity Term, said license shall become nonexclusive and continue indefinitely.

3.3 STANFORD additionally grants, and RIGEL hereby accepts, a worldwide, nonexclusive license in the Licensed Field of Use under STANFORD's right, title and interest in the Licensed Know-How other than the Vector Libraries to make, use, sell, offer for sale and import Licensed Product(s). The term of such nonexclusive license shall commence upon the Effective Date and continue indefinitely.

3.4 Notwithstanding the Exclusive license granted to RIGEL, pursuant to Sections 3.1 and 3.2, STANFORD shall have the right to practice the Licensed Patents and to use the Vector Libraries for non-commercial, academic research purposes.

4. GOVERNMENT RIGHTS.

This Agreement is subject to all of the terms and conditions of Title 35 United States Code Sections 200 through 204, including an obligation that Licensed Product(s) sold or produced in the United States be "manufactured substantially in the United States," and RIGEL agrees to take all reasonable action necessary on its part as licensee to enable STANFORD to satisfy its obligation thereunder, relating to the Invention. STANFORD agrees to provide reasonable assistance to RIGEL in the event RIGEL decides to seek a waiver under such domestic manufacture requirement.

5. DILIGENCE.

5.1 As an inducement to STANFORD to enter into this Agreement, RIGEL agrees to use all reasonable efforts and diligence to proceed with the development, manufacture, and sale of Licensed Product(s) and to diligently develop markets for the Licensed Product(s). RIGEL shall demonstrate such diligence to STANFORD by achieving proof of principle through written documentation of the following within eighteen (18) months after the Effective Date:

(a) Construction of a retroviral vector library;

(b) Infection of cells with such vector library;

(c) Detection of a physiological response to such infection in an infected cell; and

(d) Isolation and analysis of the peptide eliciting such physiological response from the cell.

5.2 If RIGEL is unable to demonstrate the foregoing proof of principle within eighteen (18) months after the Effective Date, STANFORD may elect to narrow the definition of the Licensed Field of Use to include only the use of retrovirally mediated nucleic acid libraries for drug development, drug delivery, drug screening, and target analysis and discovery, by providing written notice to RIGEL thereof. Additionally, RIGEL shall provide to STANFORD within eighteen (18) months after the Effective Date a plan for the development and commercialization of Licensed Products (a "Development Plan"). STANFORD shall comment upon and approve such plan, which approval shall not be unreasonably withheld. After the Development Plan is approved by STANFORD, RIGEL shall use reasonable efforts to diligently perform its obligations under such Development Plan. If Stanford reasonably believes that RIGEL is not using reasonable efforts to perform the Development Plan, STANFORD may so notify RIGEL. The parties shall promptly thereafter meet to discuss RIGEL's progress under the Development Plan, and shall develop a mutually agreeable plan for remedying any such lack of diligence (the "Proposed Remedy"). If RIGEL fails to perform the Proposed Remedy within one hundred and eighty (180) days after the Proposed Remedy is agreed upon, STANFORD may elect to narrow the definition of the Licensed Field of Use to include only the use of retrovirally mediated nucleic acid libraries for drug development, drug delivery, and target analysis and discovery by providing written notice to RIGEL. If RIGEL then fails to perform the Proposed Remedy within ninety (90) days after receiving STANFORD's notice that it has elected to so narrow the

Licensed Field of Use definition, then STANFORD may elect to convert the Exclusive License granted to RIGEL pursuant to Sections 3.1 and 3.2 to a nonexclusive license for the remaining term of this Agreement.

5.3 PROGRESS REPORT. On or before each anniversary of the Effective Date until RIGEL markets a Licensed Product(s), RIGEL shall make a written annual report to STANFORD covering RIGEL's progress during the preceding year toward commercial use of Licensed Product(s). Such report shall include, as a minimum, information sufficient to enable STANFORD to satisfy relevant reporting requirements of the U.S. Government and to ascertain RIGEL's progress toward meeting the diligence requirements of this Article 5.

6. ROYALTIES.

6.1 RIGEL agrees to pay to STANFORD a noncreditable, nonrefundable license issue royalty of [text omitted in original signature document] half of which shall be paid within forty-five (45) days after the Effective Date and the balance of which shall be on the first anniversary of the Effective Date.

6.2 Upon each anniversary of the Effective Date, RIGEL shall also pay to STANFORD a Minimum Annual Royalty as follows:

Anniversary of Effective Date	Minimum Annual Royalty Due
First and Second	[text omitted in original signature document]
Third through Seventh	[text omitted in original signature document]

Eighth and Thereafter	[text omitted in original signature document]

Said Minimum Annual Royalty payments are nonrefundable but they are creditable against earned royalties to the extent provided in Paragraph 6.5. The foregoing Minimum Annual Royalty payment shall be decreased by fifty percent (50%) if either:

(i) Stanford abandons all patent applications from which Licensed Patent(s) could issue prior to the time that any Licensed Patent(s) issue; or

(ii) Stanford elects to narrow the definition of the Licensed Field of Use pursuant to Section 5.2.

6.3 If Rigel grants to a third party a sublicense under the Licensed Technology solely for research, and not commercialization purposes (a "Research Sublicense"), Rigel shall also pay to STANFORD a milestone payment equal to [text omitted in original signature document] of any research milestone payment that RIGEL receives as consideration for the grant of such Research Sublicense. RIGEL shall pay such amount to STANFORD within sixty (60) days after RIGEL receives such research milestone payment.

If RIGEL grants to a third party a sublicense under the Licensed Technology which includes the right to sell and offer for sale Licensed Products (a "Commercialization Sublicense"), RIGEL shall pay to STANFORD a sublicense fee as follows:

First Sublicense Granted	[text omitted in original signature document]
Second Sublicensed Granted	[text omitted in original signature document]
Each Additional Sublicense Granted	[text omitted in original signature document]

RIGEL shall pay such sublicense fees to STANFORD within sixty (60) days after the effective date of each Commercialization Sublicense.

6.4 In addition, RIGEL shall pay STANFORD earned royalties equal to [text omitted in original signature document] of Net Sales of Licensed Products set forth in Sections 2.5(a) and 2.5(b), or [text omitted in original signature document] of Net Sales of Licensed Products which can only be categorized under Section 2.5(c). If a Licensed product can be included in more than one of Sections 2.5(a), 2.5(b) or 2.5(c), the royalty rate due to STANFORD on Net Sales of such Licensed Product shall be [text omitted in original signature document].

6.5 As further consideration for the license granted to RIGEL under this Agreement, RIGEL shall issue to STANFORD [text omitted in original signature document] shares of Preferred Stock of RIGEL, pursuant to a Stock Purchase Agreement. If such number of shares shall equal less than [text omitted in original signature document] of the total outstanding shares of RIGEL's stock at any time during the period from the date of issuance of such stock until one (1) year thereafter, STANFORD and RIGEL shall discuss whether RIGEL shall adjust the number of shares issued to Stanford under this Section 6.5.

6.6 Creditable payments under this Agreement shall be an offset to RIGEL against up to fifty percent (50%) of each earned royalty payment which RIGEL would be required to pay pursuant to Paragraph 6.4 until the entire creditable amount is exhausted.

6.7 If this Agreement is not terminated in accordance with other provisions hereof, RIGEL's obligation to pay royalties hereunder shall continue until ten (10) years after first commercial sale of Licensed Products.

6.8 The royalty on sales in currencies other than U.S. Dollars shall be calculated using the appropriate foreign exchange rate for such currency quoted by the Bank of America (San Francisco) foreign exchange desk, on the close of business on the last banking day of each calendar quarter. Royalty payments to STANFORD shall be in U.S. Dollars. All non-U.S. taxes related to royalty payments shall be paid by RIGEL and are not deductible from the payments due STANFORD.

6.9 Within thirty (30) days after receipt of a statement from STANFORD, RIGEL shall reimburse STANFORD for all costs incurred by STANFORD, including those costs incurred prior to the Effective Date, in connection with the preparation, filing and prosecution of all patent applications and maintenance of patents claiming the Invention.

7. PATENT RIGHTS.

STANFORD shall have the obligation to file, prosecute and maintain all

patent applications and patents included in the Licensed Patents. STANFORD will provide RIGEL

with an opportunity to review and comment upon the prosecution strategy and to consult with STANFORD on the content of patent filings, and will provide copies of any correspondence relating to patent applications and patents included in the Licensed Patents to RIGEL or a designee of RIGEL. RIGEL shall have the right to designate, in its sole discretion, those foreign countries in which STANFORD will file, prosecute and maintain patents and patent applications included in the Licensed Patents. STANFORD may propose to file, prosecute and maintain a Licensed Patent in a country which RIGEL has not designated pursuant to this Section 7. If RIGEL agrees to such designation, it shall reimburse STANFORD costs of such filing, prosecution of maintenance of such patent or patent applications pursuant to Section 6.9 and such patent or patent applications shall be included in the Licensed Patents. If RIGEL does not agree to such proposal, STANFORD may elect to proceed with such filing, prosecution or maintenance at its own expense, and such patent or patent application shall not be included in the Licensed Patents.

8. ROYALTY REPORTS, PAYMENTS, AND ACCOUNTING.

8.1 QUARTERLY EARNED ROYALTY PAYMENT AND REPORT. Beginning with the first sale of a Licensed Product, RIGEL shall make written reports (even if there are no sales) and earned royalty payments to STANFORD within thirty (30) days after the end of each calendar quarter. This report shall be in the form of the report of Exhibit B and shall state the number, description, and aggregate Net Sales of Licensed Product(s) during such completed calendar quarter, and resulting calculation pursuant to Paragraph 6.4 of earned royalty payment due STANFORD for such completed calendar quarter. Concurrent with the making of each such report, RIGEL shall include payment due STANFORD of royalties for the calendar quarter covered by such report.

8.2 ACCOUNTING. RIGEL agrees to keep and maintain records for a period of three (3) years showing the manufacture, sale, use, and other disposition of products sold or otherwise disposed of under the license herein granted. Such records will include general ledger records showing cash receipts and expenses, and records which include production records, customers serial numbers and related information in sufficient detail to enable the royalties payable hereunder by RIGEL to be determined. RIGEL further agrees to permit its books and records to be examined by STANFORD from time to time to the extent necessary to verify reports provided for in Paragraph 8.1. Such examination is to be made by STANFORD or its designee, at the expense of STANFORD, except in the event that the results of the audit reveal an underreporting of royalties due STANFORD of five percent (5%) or more, then the audit costs shall be paid by RIGEL.

9. NEGATION OF WARRANTIES.

9.1 Nothing in this Agreement is or shall be construed as:

(a) A warranty or representation by STANFORD as to the validity or scope of any Licensed Patent(s);

(b) A warranty or representation that anything made, used, sold, or otherwise disposed of under any license granted in this Agreement is or will be free from infringement of patents, copyrights, and other rights of third parties;

(c) An obligation to bring or prosecute actions or suits against third parties for infringement, except to the extent and in the circumstances described in Article 13;

(d) Granting by implication, estoppel, or otherwise any licenses or rights under patents or other rights of STANFORD or other persons other than Licensed Patent(s), regardless of whether such patents or other rights are dominant or subordinate to any Licensed Patent(s); or

(e) An obligation to furnish any technology or technological information other than the Licensed Technology.

9.2 Except as expressly set forth in the Agreement STANFORD MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE LICENSED PRODUCT(S)

WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER RIGHTS, OR ANY OTHER EXPRESS OR IMPLIED WARRANTIES.

9.3 RIGEL agrees that nothing in this Agreement grants RIGEL any express or implied license or right under or to:

(a) U.S. Patent No. 4,237,224, "Process for Producing Biologically Functional Molecular Chimeras"; U.S. Patent No. 4,468,464 and U.S. Patent No. 4,740470, both entitled, "Biologically Functional Molecular Chimeras" (collectively known as the Cohen/Boyer patents), or reissues thereof; or

(b) U.S. Patent 4,656,134 "Amplification of Eucaryotic Genes" or any patent application corresponding thereto.

9.4 STANFORD represents and warrants that it has all right, power and authority necessary to grant the licenses set forth in Article 3 to RIGEL, and that it has not, and will not during the term of this Agreement, grant any right to any third party which would conflict with the rights granted to RIGEL hereunder.

10. INDEMNITY.

10.1 RIGEL agrees to indemnify, hold harmless, and defend STANFORD and Stanford Health Services and their respective trustees, officers, employees, students, and agents against any and all claims by third parties for death, illness, personal injury, property damage, and improper business practices arising out of the manufacture, use, sale, or other disposition of

the Invention, Licensed Technology, or Licensed Product(s) by RIGEL or RIGEL's sublicensee(s) or customers.

10.2 STANFORD shall not be liable for any indirect, special, consequential or other damages whatsoever, whether grounded in tort (including negligence), strict liability, contract or otherwise. STANFORD shall not have any responsibilities or liabilities whatsoever with respect to Licensed Product(s).

10.3 RIGEL shall at all times comply, through insurance or self-insurance, with all statutory workers' compensation and employers' liability requirements covering any and all employees with respect to activities performed under this Agreement.

10.4 In addition to the foregoing, RIGEL shall maintain Comprehensive General Liability Insurance including Products Liability Insurance, with reputable and financially secure insurance carrier(s) to cover the activities of RIGEL and its sublicensee(s) in the amounts and during the periods specified herein. Such insurance shall provide minimum limits of liability of One Million Dollars ($1,000,000) as of the first anniversary of the date upon which RIGEL first leases a facility in which it will conduct research and development activities, and of Five Million Dollars ($5,000,000) as of the commencement of human clinical trials of Licensed Products. Such insurance shall include STANFORD, Stanford Health Services, their trustees, directors, officers, employees, students, and agents as additional insureds. Such insurance shall be written to cover claims incurred, discovered, manifested, or made during or after the expiration of this Agreement. At STANFORD's request, RIGEL shall furnish a Certificate of Insurance evidencing primary coverage and requiring thirty (30) days prior written notice of cancellation or material change to STANFORD. RIGEL shall advise STANFORD, in writing, that it maintains excess liability coverage (following form) over primary insurance for at least the minimum limits set forth above. All such insurance of RIGEL shall be primary coverage; insurance of STANFORD or Stanford Health Services shall be excess and noncontributory.

11. MARKING.

Prior to the issuance of patents on the Invention, RIGEL agrees to mark Licensed Product(s) (or their containers or labels) made, sold, or otherwise disposed of by it under the licenses granted in this Agreement with the words "Patent Pending," and following the issuance of one or more patents, with the numbers of the Licensed Patent(s).

12. STANFORD NAMES AND MARKS.

RIGEL agrees not to identify STANFORD in any promotional advertising or other promotional materials to be disseminated to the pubic or any portion thereof or to use the name of any STANFORD faculty member, employee, or student or any trademark, service mark, trade name, or symbol of STANFORD or the Stanford University Hospital, or that is associated with either of them, without STANFORD's prior written consent, except as required by law. STANFORD shall not unreasonably hold consent under this Section 12.

13. INFRINGEMENT BY OTHERS: PROTECTION OF PATENTS.

13.1 RIGEL shall promptly inform STANFORD of any suspected infringement of any Licensed Patent(s) by a third party. During the Exclusive period of this Agreement, STANFORD and RIGEL each shall have the right to institute an action for infringement of the Licensed Patent(s) against such third party in accordance with the following:

(a) If STANFORD and RIGEL agree to institute suit jointly, the suit shall be brought in both their names, the out-of-pocket costs thereof shall be borne equally, and any recovery or settlement shall be shared equally. RIGEL and STANFORD shall agree to the manner in which they shall exercise control over such action. STANFORD may, if it so desires, also be represented by separate counsel of its own selection, the fees for which counsel shall be paid by STANFORD;

(b) In the absence of agreement to institute a suit jointly, STANFORD may institute suit, and, at its option, join RIGEL as a plaintiff. If STANFORD decides to institute suit, then it shall notify RIGEL in writing. STANFORD shall bear the entire cost of such litigation and shall be entitled to retain the entire amount of any recovery or settlement; and

(c) In the absence of agreement to institute a suit jointly and if STANFORD notifies RIGEL that it has decided not to join in or institute a suit, as provided in (a) or (b) above, RIGEL may institute suit and, at its option, join STANFORD as a plaintiff. RIGEL shall bear the entire cost of such litigation and shall be entitled to retain the entire amount of any recovery or settlement, provided, however, that any recovery in excess of litigation costs shall be deemed to be Net Sales, and RIGEL shall pay STANFORD royalties thereon at the rates specified herein.

13.2 Should either STANFORD or RIGEL commence a suit under the provisions of Paragraph 13.1 and thereafter elect to abandon the same, it shall give timely notice to the other party who may, if it so desires, continue prosecution of such suit, provided, however, that the sharing of expenses and any recovery in such suit shall be as agreed upon between STANFORD and RIGEL.

14. SUBLICENSE(S).

14.1 RIGEL may grant sublicense(s) under its Exclusive license rights during the Exclusivity Term. RIGEL may grant sublicense(s) under nonexclusive license rights, if such sublicense is in conjunction with a sublicense of other RIGEL proprietary technology.

14.2 If RIGEL is unable or unwilling to serve or develop a potential market or market territory for which there is a willing sublicense(s), RIGEL will, at STANFORD's request negotiate in good faith a sublicense(s) hereunder on commercially reasonable terms.

14.3 Any sublicense(s) granted by RIGEL under this Agreement shall be subject and subordinate to terms and conditions of this Agreement, except:

(a) Sublicense terms and conditions shall reflect that any sublicensee(s) shall not grant a sublicense to a third party; and

(b) The earned royalty rate specified in the sublicense(s) may be at higher rates than the rates in this Agreement.

Any such sublicense(s) also shall expressly include the provisions of Articles 8, 9, and 10 for the benefit of STANFORD and provide for the transfer of all obligations including the payment of royalties specified in such sublicense(s), to STANFORD or its designee, in the event that this Agreement is terminated.

14.4 RIGEL agrees to provide STANFORD a copy of any sublicense(s) granted pursuant to this Article 14.

15. TERMINATION.

15.1 RIGEL may terminate this Agreement by giving STANFORD notice in writing at least thirty (30) days in advance of the Effective Date of termination selected by RIGEL.

15.2 STANFORD may terminate this Agreement if RIGEL:

(a) Is in default in payment of royalty or providing of reports;

(b) Is in material breach of any provision hereof; or

(c) Intentionally provides any false report;

and RIGEL fails to remedy any such default, breach, or false report within thirty (30) days after written notice thereof by STANFORD.

15.3 SURVIVING ANY TERMINATION ARE:

(a) RIGEL's obligation to pay royalties accrued or accruable;

(b) Any cause of action or claim of RIGEL or STANFORD, accrued or to accrue, because of any breach or default by the other party; and

(c) The provisions of Articles 8, 9, and 10.

16. ASSIGNMENT.

This Agreement may not be assigned by either party without the express written consent of the other party, except that RIGEL may assign the Agreement in connection with a merger, consolidation or sale of all or substantially all of RIGEL's assets.

17. DOUBLE PATENTING CONTINGENCY.

If the PTO rejects either the Nolan/Rothenberg Patent Application for double patenting in view of the claims of the Nolan Patent Application, or the claims of the Nolan Patent Application for double patenting in view of the claims of the Nolan/Rothenberg Patent Application, then RIGEL may elect to assign its right, title and interest in the Nolan Patent Application to STANFORD, in which case STANFORD shall grant to RIGEL an irrevocable, exclusive, worldwide, royalty-free license under STANFORD's right, title and interest in the Nolan Patent Application for all purposes.

18. ARBITRATION.

18.1 Any controversy arising under or related to this Agreement, and any disputed claim by either party against the other under this Agreement excluding any dispute relating to patent validity or infringement arising under this Agreement, shall be settled by arbitration in accordance with the Licensing Agreement Arbitration Rules of the American Arbitration Association.

18.2 Upon request by either party, arbitration will be by a third party arbitrator mutually agreed upon in writing by RIGEL and STANFORD within thirty (30) days of such arbitration request. Judgement upon the award rendered by the arbitrator shall be final and nonappealable and may be entered in any court having jurisdiction thereof.

18.3 The parties shall be entitled to discovery in like manner as if the arbitration were a civil suit in the California Superior Court.

18.4 Any arbitration shall be held at Stanford, California, unless the parties hereto mutually agree in writing to another place.

19. NOTICES.

All notices under this Agreement shall be deemed to have been fully given when done in writing and deposited in the United States mail registered or certified, and addressed as follows:

To STANFORD: Office of Technology Licensing
Stanford University
900 Welch Road, Suite 350
Palo Alto, CA 94304-1850

Attention: Director

To RIGEL: 24 Windsor Drive
Hillsborough, CA 94010

Attention: Dr. Donald G. Payan

Either party may change its address upon written notice to the other party.

20. WAIVER

None of the terms of this Agreement can be waived except by the written consent of the party waiving compliance.

21. APPLICABLE LAW.

This Agreement shall be governed by the laws of the State of California applicable to agreements negotiated, executed and performed wholly within California.

22. SEVERABILITY.

If any provision or provisions of this Agreement shall be held to be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not be in any way affected or impaired thereby.

23. ENTIRE AGREEMENT.

This Agreement, together with the Exhibits attached hereto, embodies the entire understanding of the parties and shall supercede all previous communications, representations or understandings, either oral or written, between the parties relating to the subject matter hereof. No amendment or modification hereof shall be valid or binding upon the parties unless made in writing and signed by duly authorized representatives of both parties.

24. COUNTERPARTS.

This Agreement may be executed in counterparts, with the same force and effect as if the parties had executed the same instrument.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement in duplicate originals by their duly authorized officers or representatives.

THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY

Signature /s/ Katherine Ku

Name Katherine Ku

Title Director, Technology Licensing

Date October 7, 1996

RIGEL

Signature /s/ Donald G. Payan

Name Donald G. Payan

Title President & CEO

Date 10/9/96

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EXHIBIT A

MATERIALS FROM NOLAN LAB TO BE LICENSED TO RIGEL

VECTOR LIBRARIES

1. Random peptide library in pMSCU & Bst X1
2. SH-3 first generation library
3. CPP32 inhibitor peptide library
4. SH-3 second generation library
5. Coiled-coil library

PLASMIDS

1. pMSCU SD & Bst X1
2. pBabc Pur
3. pMSCU SD - IRES neo Bst X1
4. p5 & MD

CELL LINES

1. phiNX cell lines - gp, eco, ampho
2. 293 T

EXHIBIT B

SAMPLE REPORTING FORM

Stanford Docket No. S_____-_____

This report is provided pursuant to the license agreement between Stanford University and _____.

License Agreement Effective Date: _____

Report Covering Period	_____
Fixed Fees (Annual Minimum Payment)	$_____
Number of Sublicenses Executed	_____
Net Sales	$_____
Royalty Calculation	_____
Royalty Subtotal	$_____
Credit	$_____
Royalty Due	$_____

Comments:

AMENDMENT

The Board of Trustees of the Leland Stanford Junior University ("Stanford") and Rigel Pharmaceuticals, Inc. ("Rigel") agree to extend the time period within which Rigel must pay the license issue royalty due to Stanford pursuant to the License Agreement between Stanford and Rigel dated October 7, 1996 (the "Agreement"). Section 6.1 of the Agreement is hereby amended to provide that Rigel will pay the license issue royalty to Stanford within ninety (90) days after the Effective Date of the Agreement.

Accepted and agreed by:

/s/ Katherine Ku	/s/ Donald G. Payan
- ----------	----------
Ms. Katherine Ku; Director, Technology Licensing Stanford University	Dr. Donald G. Payan Rigel Pharmaceuticals, Inc.
December 6, 1996	November 25, 1996
- ----------	----------
Date	Date

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LICENSE AGREEMENT

Effective as of August 18, 1997 (the "Effective Date"), THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, a body having corporate powers under the laws of the State of California ("STANFORD") and RIGEL PHARMACEUTICALS, INC., a Delaware corporation having a principle place of business at 772 Lucerne Drive, Sunnyvale, CA 94086 ("RIGEL"), agree as follows:

1. BACKGROUND.

1.1 STANFORD owns certain Phoenix and 293T cell lines and derivatives thereof developed in the laboratories of Dr. Garry Nolan and Dr. Michele Calos at STANFORD.

1.2 STANFORD has previously granted to RIGEL a nonexclusive license to such materials pursuant to the License Agreement between RIGEL and STANFORD dated October 7, 1996 (the "1996 License Agreement").

1.3 RIGEL now desires to obtain an exclusive worldwide license to such materials for all uses in the RIGEL Field (as defined below), which exclusive license shall be in addition to the nonexclusive license provided in the 1996 License Agreement.

2. DEFINITIONS.

2.1 "EXCLUSIVE" means that, subject to Article 3, STANFORD shall not grant further licenses in the RIGEL Field.

2.2 "GENE THERAPY" means the treatment of cells which are contained within a human subject or which are subsequently transplanted into a human subject with the Materials.

2.3 "LICENSED PRODUCT(S)" means any product in the RIGEL Field which: (i) directly incorporates any of the Materials; or (ii) would not, but for the use of the Materials, have been identified, discovered or developed. Licensed Products shall include without limitation both diagnostic and therapeutic pharmaceutical products.

2.4 "MATERIALS" means the PhiNX helper-free retrovirus producer lines, PhiNX ampho and PhiNX eco (collectively, the "Phoenix cell lines") and the 293T cell lines developed in the laboratories of Dr. Garry Nolan and Dr. Michele Calos at STANFORD.

2.5 "RIGEL FIELD" means the creation and use of retrovirally produced peptide and protein libraries of random sequence for the screening of transdominant effector peptides and RNA molecules as claimed in U.S. Patent Application Serial No. 589911/PCT No. 9701019 (entitled "Methods for Screening for Transdominant Intracellular Effector Peptides and RNA Molecules") as such claims were filed on January 23, 1997, and U.S. Patent Application Serial No. 589109/PCT No. 9701048 (entitled "Methods for Screening for Transdominant

Effector Peptides and RNA Molecules"), as such claims were filed on January 23, 1997, as well as any

processes, techniques and applications disclosed in the foregoing patent applications, for drug discovery and therapeutic target identification.

2.6 "NET SALES" means the gross revenue derived by RIGEL and/or RIGEL's sublicensees from the sales of Licensed Product(s), less the following items insofar as they actually pertain to the disposition of such Licensed Product(s) by RIGEL or RIGEL's sublicensees, are included in such gross revenue, and are separately billed.

(a) Import, export, excise and sales taxes, and custom duties;

(b) Credit for returns, allowances, trades or retroactive price adjustments;

(c) Transportation charges, issuance and allowances;

(d) Discounts actually allowed; or

(e) Royalties payable to third parties on the manufacture, use, sale offer for sale or import of Licensed Products.

3. GRANT; TRANSFER OF MATERIALS.

3.1 STANFORD hereby grants, and RIGEL hereby accepts, a worldwide, royalty-bearing, sublicensable license in the RIGEL Field under STANFORD's right, title and interest in the Materials to make, use, sell, offer for sale and import Licensed Products.

3.2 The license granted in Section 3.1 is Exclusive, including the right to sublicense pursuant to Article 12, in the RIGEL Field for a term (the "Exclusivity Term") commencing as of the Effective Date and ending three (3) years thereafter with respect to both the 293T and Phoenix cell lines; provided, however, that RIGEL may extend such Exclusivity Term with respect to either or both of such cell lines as follows: If RIGEL elects to extend the Exclusivity Term with respect to the 293T cell line for an additional year, RIGEL shall pay to STANFORD an exclusivity extension fee of [text omitted in original signature document] (the "293T Exclusivity Extension Fee"). If RIGEL elects to extend the Exclusivity Term with respect to the Phoenix cell line for an additional year, RIGEL shall pay to STANFORD an exclusivity extension fee of [text omitted in original signature document] (the "Phoenix Exclusivity Extension Fee"). Such exclusivity extension fees shall be due any time prior to the third anniversary of the Effective Date, and shall operate to extend the Exclusivity Term until the fourth anniversary of the Effective Date with respect to the 293T cell line, if RIGEL pays the 293T Exclusivity Extension Fee, and/or the Phoenix cell line, if RIGEL pays the Phoenix Exclusivity Extension Fee. RIGEL may elect to extend the Exclusivity Term for additional one year periods of time with respect to the 293T cell line and/or the Phoenix cell line, as applicable, by so notifying STANFORD of its intent to extend the Exclusivity Term with respect to the 293T cell line and/or the Phoenix cell line at least thirty (30) days prior to the following anniversary of the Effective Date and paying to STANFORD either or both of the 293T Exclusivity Extension Fee and the Phoenix Extension Fee, as applicable, prior to the following anniversary of the Effective Date. Any exclusivity extension fees paid by RIGEL pursuant to this Section 3.2 shall be nonrefundable but creditable against

earned royalties as provided in Section 6.4. If RIGEL extends the Exclusivity Term, RIGEL and STANFORD shall discuss in good faith additional appropriate diligence milestones.

3.3 After expiration of the Exclusivity Term with respect to the 293T cell line and/or the Phoenix cell line, the license granted to RIGEL pursuant to Section 3.1 with respect to such cell line(s), shall terminate. Such termination shall not affect the term of the nonexclusive license granted to RIGEL under the 1996 License Agreement.

3.4 Notwithstanding the Exclusive license granted to RIGEL pursuant to Section 3.1, STANFORD shall have the right to use and to distribute the Materials to other nonprofit and academic institutions for non-commercial, academic research purposes in the RIGEL Field. Any transfer of the Materials by STANFORD pursuant to this Section 3.4 shall be governed by a material transfer agreement which (i) restricts the recipient's use of the Materials to the performance of specified academic research projects, (ii) does not allow the recipient to transfer the Materials to any other entity, and (iii) contains

other terms and conditions typically included in agreements governing the transfer and use of biological materials for noncommercial academic research purposes.

3.5 Promptly after the Effective Date, STANFORD shall transfer to RIGEL such quantities of the Materials as RIGEL shall reasonably request. Thereafter, STANFORD shall transfer to RIGEL such additional quantities of Materials as RIGEL shall reasonably request in the event that RIGEL's stock of the Materials is destroyed or contaminated.

4. GOVERNMENT RIGHTS.

This Agreement is subject to all of the terms and conditions of Title 35 United States Code Sections 200 through 204, including an obligation that Licensed Product(s) sold or produced in the United States be "manufactured substantially in the United States," and RIGEL agrees to take all reasonable action necessary on its part as licensee to enable STANFORD to satisfy its obligation thereunder. STANFORD agrees to provide reasonable assistance to RIGEL in the event RIGEL decides to seek a waiver under such domestic manufacture requirement.

5. DILIGENCE.

5.1 As an inducement to STANFORD to enter into this Agreement, RIGEL agrees to use all reasonable efforts and diligence to proceed with the development, manufacture and sale of Licensed Product(s) and to develop diligently markets for the Licensed Product(s). RIGEL shall demonstrate such diligence to STANFORD by achieving proof of principle though written documentation of the following achievements:

(a) Construction of a retroviral vector library;

(b) Infection of cells with such vector library;

(c) Detection of a physiological response to such infection in an infected cell;

(d) Isolation and analysis of the peptide eliciting such physiological response from the cell; and

(e) Identification of two novel targets for drug design, or demonstration that two previously known targets have a novel activity suitable for drug design.

5.2 If RIGEL is unable to demonstrate items 5.1(a) through (d) within eighteen (18) months after the Effective Date, and item 5.1(e) within thirty six (36) months after the Effective Date, STANFORD may request that RIGEL meet with STANFORD to discuss RIGEL's lack of diligence. The parties shall meet within thirty (30) days after RIGEL receives any such notice to develop a mutually agreeable plan for remedying any such lack of diligence (the "Proposed Remedy"). If RIGEL fails to perform the Proposed Remedy within one hundred eighty (180) days after the Proposed Remedy is agreed upon, STANFORD may elect to terminate this Agreement, which termination shall not have any effect upon the rights granted to RIGEL pursuant to the 1996 License Agreement.

5.3 On or before each anniversary of the Effective Date during the Exclusivity Term, RIGEL shall make a written annual report to STANFORD covering RIGEL's progress during the preceding year toward commercial use of the Licensed Product(s). Such report shall include as a minimum information sufficient to enable STANFORD to satisfy relevant reporting requirements of the U.S. Government and to ascertain RIGEL's progress toward meeting the diligence requirements of this Article 5.

6. LICENSE FEE AND ROYALTIES.

6.1 In partial consideration for the Exclusive License granted by STANFORD to RIGEL with respect to the Phoenix cell lines included in the Materials, RIGEL agrees to pay to STANFORD the following:

(a) A noncreditable, nonrefundable license issue royalty of [text omitted in original signature document], which amount shall be paid within thirty (30) days after the Effective Date.

(b) An exclusivity fee equal to [text omitted in original signature document] for each of the three (3) years following the first anniversary of the Effective Date, which amounts shall be paid to STANFORD within thirty (30) days after each of the first, second and third anniversaries of the Effective Date. Such payments shall be nonrefundable but creditable against earned royalties to the extent provided in Section 6.4.

(c) RIGEL shall issue to STANFORD [text omitted in original signature document] Stock of RIGEL, pursuant to a stock purchase agreement to be entered into between RIGEL and STANFORD within ninety (90) days after the Effective Date.

(d) If RIGEL grants to a third party a sublicense to the Materials solely for research, and not commercialization purposes (a "Research Sublicense"), RIGEL shall also pay to STANFORD a milestone payment equal to [text omitted in original signature document] payment that

RIGEL receives as consideration for the grant of such Research Sublicense. RIGEL shall pay such amount to STANFORD within sixty (60) days after RIGEL receives such research milestone payment. If RIGEL grants to a third party a sublicense under the Materials which includes the right to sell and offer for sale Licensed Products (a "Commercialization Sublicense"), RIGEL shall pay to STANFORD a sublicense fee as follows:

First Commercialization Sublicense Granted	[text omitted in original signature document]
Second Commercialization Sublicense Granted	[text omitted in original signature document]
Each Additional Commercialization Sublicense Granted	[text omitted in original signature document]

If RIGEL owes amounts to STANFORD pursuant to this Section 6.1(d) and also pursuant to Section 6.3 of the 1996 License Agreement with respect to a particular Research Sublicense or Commercialization Sublicense, the amounts due to STANFORD pursuant to this Section 6.1(d) shall be reduced by any amounts due to STANFORD pursuant to Section 6.3 of the 1996 License Agreement with respect to such Research Sublicense or Commercialization Sublicense. RIGEL shall pay such sublicense fees to STANFORD within sixty (60) days after the effective date of each Commercialization Sublicense.

6.2 In partial consideration for the Exclusive License granted by STANFORD to RIGEL for the 293T cell lines included in the Materials, RIGEL agrees to pay to STANFORD an exclusivity fee equal to [text omitted in original signature document] for each of the three (3) years following the first anniversary of the Effective Date, which amounts shall be paid to STANFORD within thirty (30) days after each of the first, second and third anniversaries of the Effective Date. Such payments shall be nonrefundable but creditable against earned royalties to the extent provided in Section 6.4.

6.3 As further consideration for the license granted to RIGEL pursuant to Section 3.1, RIGEL shall pay to STANFORD earned royalties equal to [text omitted in original signature document] of Net Sales of Licensed Products by RIGEL and its sublicensees; provided, however, that if royalties on Net Sales of a particular Licensed Product by RIGEL and its sublicensees would be due to STANFORD pursuant to both this Section 6.3 and Section 6.4 of the 1996 License Agreement, RIGEL shall be obligated to pay only the royalties due to STANFORD pursuant to Section 6.4 of the 1996 License Agreement on Net Sales of such Licensed Products.

6.4 Creditable payments under this Agreement shall be an offset to RIGEL against up to fifty percent (50%) of each earned royalty payment which RIGEL would be required to pay pursuant to Section 6.4 until the entire creditable amount is exhausted.

6.5 If this Agreement is not terminated in accordance with other provisions hereof, RIGEL's obligation to pay royalties pursuant to Section 6.3 shall continue until ten (10) years after first commercial sale of Licensed Products.

6.6 The royalties on sales in currencies other than U.S. Dollars shall be calculated using the appropriate foreign exchange rate for such currency quoted by the Bank of America (San Francisco) foreign exchange desk, on the close of business on the last banking day of each calendar quarter. Royalty payments to STANFORD shall be in U.S. Dollars. All non-U.S. taxes related to royalty payments shall be paid by RIGEL and are not deductible from the payments due STANFORD.

7. Royalty Reports, Payments, and Accounting.

7.1 QUARTERLY EARNED ROYALTY PAYMENT AND REPORT. Beginning with the first sale of a Licensed Product, RIGEL shall make written reports (even if there are no sales in a particular quarter) and earned royalty payments to STANFORD within thirty (30) days after the end of each calendar quarter. This report shall be in the form of the report of Exhibit A and shall state the number, description, and aggregate Net Sales of Licensed Product(s) during such

completed calendar quarter, and resulting calculation pursuant to Section 6.3 of earned royalty payments due STANFORD for such completed calendar quarter. Concurrent with the making of each such report, RIGEL shall include payment due STANFORD of earned royalties for the calendar quarter covered by such report.

7.2 ACCOUNTING. RIGEL agrees to keep and maintain records for a period of three (3) years showing the manufacture, sale, use, and other disposition of products sold or otherwise disposed of under the license herein granted. Such records will include general ledger records showing cash receipts and expenses, and records which include production records, customers serial numbers and related information in sufficient detail to enable the royalties payable hereunder by RIGEL to be determined. RIGEL further agrees to permit its books and records to be examined by STANFORD from time to time to the extent necessary to verify reports provided for in Section 7.1. Such examination is to be made by STANFORD or its designee, at the expense of STANFORD, except in the event that the results of the audit reveal an underreporting of royalties due STANFORD of five percent (5%) or more, then the audit costs shall be paid by RIGEL.

8. PATENTS; NEW INVENTIONS.

8.1 STANFORD's Office of Technology Licensing represents and warrants that to the best of its knowledge as of the Effective Date, STANFORD has not sought or obtained patent protection of the Materials or any use thereof in the Rigel Field. STANFORD agrees that future inventions and discoveries using or relating to the Materials may be useful to RIGEL in the development and/or commercialization of Licensed Products. Subject to STANFORD's obligations with respect to sponsored research, STANFORD will, as soon as practicable, bring any such new invention or discovery to RIGEL's attention and provide RIGEL a reasonable opportunity to negotiate a license therefor.

9. WARRANTIES.

9.1 STANFORD's Office of Technology Licensing represents and warrants that as of the Effective Date, it has received no claims by third parties that the use of the Materials infringes any patents, copyrights, and other rights of third parties.

9.2 STANFORD represents and warrants that it has all right, power and authority necessary to grant the License set forth in Article 3 to RIGEL, and that it has not, and will not during the term of this Agreement, grant any right or interest in the Materials to any third party which would conflict with the rights granted to RIGEL hereunder.

9.3 RIGEL agrees that nothing in this Agreement grants RIGEL any express or implied license or right under or to:

(a) U.S. Patent No. 4,237,224, "Process for Producing Biologically Functional Molecular Chimeras"; U.S. Patent No. 4,468,464 and U.S. Patent No. 4,740,470, both entitled, "Biologically Functional Molecular Chimeras" (collectively known as the Cohen/Boyer patents), or reissues thereof; or

(b) U.S. Patent 4,656,134, entitled "Amplification of Eucaryotic Genes" or any patent application corresponding thereto.

9.4 Except as provided in Section 9.1 and as otherwise expressly set forth in this Agreement, nothing in this Agreement will be construed as a warranty or representation that anything made, used, sold, or otherwise disposed of under any license granted in this Agreement is or will be free from infringement of patents, copyrights, and trademarks of third parties; conferring rights to use in advertising, publicity, or otherwise any trademark or the name of "STANFORD"; or granting by implication, estoppel, or otherwise any licenses or rights under patents of STANFORD.

9.5 EXCEPT AS EXPRESSLY SET FORTH IN THE AGREEMENT, STANFORD MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE LICENSED PRODUCT(S) WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER RIGHTS, OR ANY OTHER EXPRESS OR IMPLIED WARRANTIES.

10. INDEMNITY.

10.1 RIGEL agrees to indemnify, hold harmless, and defend STANFORD and STANFORD Health Services (or any successor thereto) and their respective trustees, officers, employees, students, and agents against any and all claims by third parties for death, illness, personal injury, property damage, and improper business practices arising out of the manufacture, use, sale, or other disposition of the Materials or Licensed Product(s) by RIGEL or RIGEL's

sublicensee(s) or customers.

10.2 STANFORD shall not be liable for any indirect, special, consequential or other damages whatsoever, whether grounded in tort (including negligence), strict liability, contract or otherwise. STANFORD shall not have any responsibilities or liabilities whatsoever with respect to Licensed Product(s).

10.3 RIGEL shall at all times comply, through insurance or self-insurance, with all statutory workers' compensation and employers' liability requirements covering any and all employees with respect to activities performed under this Agreement.

10.4 In addition to the foregoing, RIGEL shall maintain Comprehensive General Liability Insurance, including Products Liability Insurance, with reputable and financially secure insurance carrier(s) to cover the activities of RIGEL and its sublicensee(s) in the amounts and during the periods specified herein. Such insurance shall provide minimum limits of liability of One Million Dollars ($1,000,000) as of the first anniversary of the date upon which RIGEL first leases a facility in which it will conduct research and development activities, and of Five Million Dollars ($5,000,000) as of the commencement of human clinical trials of Licensed Products. Such insurance shall include STANFORD, Stanford Health Services (or any successor thereto), their trustees, directors, officers, employees, students, and agents as additional insureds. Such insurance shall be written to cover claims incurred, discovered, manifested, or made during or after the expiration of this Agreement. At STANFORD's request, RIGEL shall furnish a Certificate of Insurance evidencing primary coverage and requiring thirty (30) days prior written notice of cancellation or material change to STANFORD. RIGEL shall advise STANFORD, in writing, that it maintains excess liability coverage (following form) over primary insurance for at least the minimum limits set forth above. All such insurance of RIGEL shall be primary coverage; insurance of STANFORD or Stanford Health Services (or any successor thereto) shall be excess and noncontributory.

11. STANFORD NAMES AND MARKS

11.1 RIGEL agrees not to identify STANFORD in any promotional advertising or other promotional materials to be disseminated to the public or any portion thereof or to use the name of any STANFORD faculty member, employee, or student or any trademark, service mark, trade name, or symbol of STANFORD or the STANFORD Health Services (or any successor thereto), or that is associated with either of them, without STANFORD's prior written consent, except as required by law. STANFORD shall not unreasonably hold consent under this Section 11.

12. SUBLICENSE(S).

12.1 RIGEL may, solely in conjunction with a sublicense under the rights licensed to RIGEL pursuant to Section 3.1 of the 1996 License Agreement, grant sublicense(s) under its Exclusive license rights during the Exclusivity Term.

12.2 Any sublicense(s) granted by RIGEL under this Agreement shall be subject and subordinate to terms and conditions of this Agreement, except:

(a) Sublicense terms and conditions shall reflect that any sublicensee(s) shall not grant a sublicense to a third party; and

(b) The earned royalty rate specified in the sublicense(s) may be at higher rates than the rates in this Agreement.

Any such sublicense(s) also shall expressly include the provisions of Articles 7, 9, and 10 for the benefit of STANFORD and provide for the transfer of all obligations including the payment of royalties specified in such sublicense(s), to STANFORD or its designee, in the event that this Agreement is terminated, if such sublicenses remain in effect after termination of this Agreement.

12.3 RIGEL agrees to provide STANFORD a copy of any sublicense(s) granted pursuant to this Article 12.

13. TERM AND TERMINATION.

13.1 The term of this Agreement shall commence upon the Effective Date and shall continue until expiration of both the Phoenix cell Exclusivity Term and the 293T cell line Exclusivity Term. Additionally, RIGEL may

terminate this Agreement prior to such expiration date by giving STANFORD notice in writing at least thirty (30) days in advance of the effective date of termination selected by RIGEL. If RIGEL terminates this Agreement prior to the third anniversary of the Effective Date, RIGEL's obligations to make the payments due to STANFORD pursuant to Sections 6.1(b), and 6.2 and shall survive such termination until expiration of RIGEL's obligations thereunder. Any termination or expiration of this Agreement shall have no effect upon the Rights granted to RIGEL pursuant to the 1996 License Agreement.

13.2 STANFORD may terminate this Agreement if RIGEL:

(a) Is in default in payment of royalty or providing of reports;

(b) Is in material breach of any provision hereof; or

(c) Intentionally provides any false report;

and RIGEL fails to remedy any such default, breach, or false report within thirty (30) days after written notice thereof to RIGEL by STANFORD.

13.3 SURVIVING ANY TERMINATION ARE:

(a) RIGEL's obligation to pay exclusivity fees pursuant to Sections 6.1(b) and 6.2, royalties accrued or accruable pursuant to Section 6.3, and Sections 6.4, 6.5 and 6.6;

(b) Any cause of action or claim of RIGEL or STANFORD, accrued or to accrue, because of any breach or default by the other party; and

(c) The provisions of Articles 7, 9 and 10.

14. ASSIGNMENT.

This Agreement may not be assigned by either party without the express written consent of the other party, except that RIGEL may assign the Agreement in connection with a merger, consolidation or sale of all or substantially all of RIGEL's assets.

15. ARBITRATION.

15.1 Any controversy arising under or related to this Agreement, and any disputed claim by either party against the other under this Agreement excluding any dispute relating to patent validity or infringement arising under this Agreement, shall be settled by arbitration in accordance with the Licensing Agreement Arbitration Rules of the American Arbitration Association.

15.2 Upon request by either party, arbitration will be by a third party arbitrator mutually agreed upon in writing by RIGEL and STANFORD within thirty (30) days of such arbitration request. Judgment upon the award rendered by the arbitrator shall be final and nonappealable and may be entered in any court having jurisdiction thereof.

15.3 The parties shall be entitled to discovery in like manner as if the arbitration were a civil suit in the California Superior Court.

15.4 Any arbitration shall be held at Stanford, California, unless the parties hereto mutually agree in writing to another place.

16. NOTICES.

All notices under this Agreement shall be deemed to have been fully given when done in writing and deposited in the United States mail registered or certified, and addressed as follows:

To STANFORD: Office of Technology Licensing
Stanford University
900 Welch Road, Suite 350
Palo Alto, CA 94304-1850

Attention: Director

To RIGEL: 772 Lucerne Drive
Sunnyvale, CA 94086

Attention: Dr. Donald G. Payan

Either party may change its address upon written notice to the other party.

17. WAIVER.

None of the terms of this Agreement can be waived except by the written consent of the party waiving compliance.

18. APPLICABLE LAW.

This Agreement shall be governed by the laws of the State of California applicable to agreements negotiated, executed and performed wholly within California. Any claim or controversy arising out of or related to this Agreement or any breach hereof shall be submitted to a court of applicable jurisdiction in the State of California, and each party hereby consents to the jurisdiction and venue of such court.

19. SEVERABILITY.

If any provision or provisions of this Agreement shall be held to be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not be in any way affected or impaired thereby.

20. ENTIRE AGREEMENT.

This Agreement, together with the Exhibit attached hereto, embodies the entire understanding of the parties and shall supersede all previous communications, representations or understandings, either oral or written, between the parties relating to the subject matter hereof. No amendment or modification hereof shall be valid or binding upon the parties unless made in writing and signed by duly authorized representatives of both parties.

21. COUNTERPARTS.

This Agreement may be executed in counterparts, with the same force and effect as if the parties had executed the same instrument.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement in duplicate originals by their duly authorized officers or representatives.

THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY

Signature /s/ Jon Sandelin

Name Jon Sandelin

Title Acting Director

Date August 18, 1997

RIGEL PHARMACEUTICALS , INC.

Signature /s/ Donald G. Payan

Name Donald G. Payan

Title VP R&D and COO

Date 8/18/97

EXHIBIT A

SAMPLE REPORTING FORM

Stanford Docket No. S____-_____

This report is provided pursuant to the license agreement between Stanford University and _____.

License Agreement Effective Date: _____

<TABLE>
<S> <C>

Report Covering Period	
Fixed Fees (Annual Minimum Payment)	$
Number of Sublicenses Executed	
Net Sales	$
Royalty Calculation	
Royalty Subtotal	$
Credit	$
Royalty Due	$

</TABLE>

<TABLE>

<S> <C>

</TABLE>

LICENSE AGREEMENT

Effective as of March 27, 1998 ("Effective Date"), THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, a body having corporate powers under the laws of the State of California ("STANFORD"), and RIGEL PHARMACEUTICALS, INC., a Delaware corporation doing business as RIGEL, INC. in California, having a principal place of business at 772 Lucerne Drive, Sunnyvale, California 94086 ("RIGEL"), agree as follows:

1. BACKGROUND

1.1 STANFORD has an assignment of U.S Provisional Applications (the "Provisionals"), Serial No. 042576, filed April 2, 1997, and Serial No. 054623, filed August 4, 1997 entitled, "Detection of Molecular Interactions by Reporter Subunit Complementation" from the laboratory of Helen M. Blau,

Ph.D. (the "Invention"), and as described in Stanford Docket S96-125, and any Licensed Patents, as hereinafter defined, which may claim such Invention.

1.2 STANFORD has certain biological materials ("Licensed BIOLOGICAL Materials") and other know-how ("Know-How"), as defined below, pertaining to the Inventions.

1.3 STANFORD desires to have the Know-How and Inventions perfected and marketed at the earliest possible time in order that products resulting therefrom may be available for public use and benefit.

1.4 RIGEL desires a license under said Know-How, Invention and Licensed Patents to develop, manufacture, use and sell Licensed Products in the Licensed Field of Use, as defined below.

1.5 The Know-How and Invention were made in the course of research supported by the National Institutes of Health.

2. DEFINITIONS

2.1 "EXCLUSIVE" means that STANFORD shall not grant further licenses in the Licensed Territory in the Licensed Field of Use.

2.2 "LICENSED BIOLOGICAL MATERIALS" means the materials listed on Exhibit A, as amended from time to time upon the parties' mutual written consent.

2.3 "LICENSED FIELD OF USE" means, subject to Section 14:

(a) the development of reporter systems useful for the analysis of protein-protein interactions;

(b) the development of methods for analyzing molecular interactions by reporter subunit complementation; and

(c) applications of the systems and methods set forth in (a) and (b) to functional genomics, target analysis and drug discovery.

2.4 "LICENSED KNOW-HOW" means know-how useful for the commercial exploitation of the Licensed Patents in the Licensed Field of Use and is provided to RIGEL by STANFORD, including know-how, trade secrets, protocols, information, processes or other subject matter which is either disclosed in the Licensed Patents, or useful to practice the Invention in the Licensed Field of Use. Licensed Know-How excludes the Licensed Patents and includes the Licensed Biological Materials. STANFORD has no obligation to provide such know-how.

2.5 "LICENSED PATENTS" means any Letters Patent issued upon (i) patent applications claiming priority from or based upon the Provisionals; (ii) any patents issuing from any divisional, continuations, substitute, or continuation-in-part (to the extent provided in this Section 2.5) application relating to the patent applications described in (i); and (iii) any foreign counterparts of the patent applications described in (i) or (ii). Continuation-in-part applications are included in the Licensed Patents to the extent that such continuation-in-part claims subject matter disclosed in the applications set forth in (i) and to the extent that the practice of an invention claimed in a Licensed Patent issuing from a patent application other than such continuation-in-part would infringe a claim of a Licensed Patent issuing from such continuation-in-part.

2.6 "LICENSED PRODUCTS" means

(a) any product, the manufacture, use, sale, offer for sale and import of which:

(i) is covered by one or more valid claims of an issued, unexpired Licensed Patent directed to the Invention. Claims of issued, unexpired Licensed Patent shall be presumed to be valid unless and until they have been held to be invalid by a final judgment of a court of competent jurisdiction from which no appeal can be or is taken; or

(ii) is covered by any claim being prosecuted in a pending application directed to the Invention, which claim has not been pending for more than three (3) years from the first filing of such claim; and

(b) any product which directly incorporates any of the Licensed Biological Materials; and

(c) any product which would not, but for the use of the Licensed Technology, have been identified, discovered or developed.

2.7 "LICENSED TECHNOLOGY" means the Licensed Patents and the Licensed Know-How.

2.8 "LICENSED TERRITORY" means all the countries in the world.

2.9 "NET SALES" means the gross revenue derived by RIGEL and/or its sublicensee(s) from the sales of Licensed Products to end users thereof, less the following items but only insofar as they actually pertain to the disposition of such Licensed Products by RIGEL or RIGEL's sublicensee(s), are included in such gross revenue, and are separately billed:

(a) import, export, excise and sales taxes, and custom duties;

(b) transportation charges, issuances and allowances;

(c) credit for returns, allowances, trades or retroactive price adjustments;

(d) discounts actually allowed; or

(e) royalties payable to third parties on the manufacture, use, sale, offer for sale or import of Licensed Products.

2.10 "SERVICE PROVIDER" means a third party contract research or similar organization that performs assay services (i) for other entities on a fee-for-service basis and (ii) not in connection with such organization's own drug development programs (whether such programs are conducted solely by such entity or jointly by such entity and one or more third parties).

3. GRANT

3.1 STANFORD hereby grants, and RIGEL hereby accepts, a license in the Licensed Field of Use to make, use, sell, offer for sale and import Licensed Products in the Licensed Territory.

3.2 RIGEL hereby grants, and STANFORD hereby accepts, a non-exclusive, royalty free license under its interest in any inventions conceived by RIGEL during the term of this Agreement that solely relate to the technology claimed in the Licensed Patents and any intellectual property rights related thereto (collectively, "Improvements"), to practice and grant licenses under such Improvements solely for noncommercial, academic research purposes.

3.3 The license granted to RIGEL pursuant to Section 3.1 under the Licensed Know-How shall be nonexclusive for the term of this Agreement. The license granted in Section 3.1 under the Licensed Patents is Exclusive for a term (the "Exclusivity Term") commencing as of the Effective Date and ending (except as otherwise provided in this Agreement) on the first to occur of the following:

(a) the fifth anniversary of the Effective Date if STANFORD does not grant a license under the Licensed Patents outside the Licensed Field of Use to a third party prior to or on such date; or

(b) the eighth anniversary of the Effective Date, if STANFORD grants a license under the Licensed Patents outside the Licensed Field of Use to a third party prior to or on the fifth anniversary of the Effective Date.

After expiration of the Exclusivity Term, the license granted to RIGEL pursuant to Section 3.1 under the Licensed Patents shall be nonexclusive for the remainder of the term of the Agreement.

3.4 Notwithstanding the Exclusive license under the Licensed Patents granted to RIGEL pursuant to Section 3.1, STANFORD shall have the right to practice the Licensed Technology in the Licensed Field of Use for noncommercial, academic research purposes. STANFORD shall have the right to publish any information included in the Licensed Technology.

3.5 STANFORD may grant sublicenses under Improvements to third parties solely for noncommercial, academic research purposes, provided that each such sublicense is granted in conjunction with a license under the Licensed Technology. After the expiration of the Exclusivity Term, STANFORD may grant sublicenses under Improvements to third parties for purposes other than conducting noncommercial academic research, provided that each such sublicense is granted solely in conjunction with the grant of a license under the Licensed Technology. STANFORD's license under Section 3.2 and its ability to grant sublicenses thereunder as provided in this Section 3.5 shall survive termination

of this Agreement.

4. GOVERNMENT RIGHTS

This Agreement is subject to all of the terms and conditions of Title 35 United States Code Sections 200 through 204, including an obligation that Licensed Products sold or produced in the United States be "manufactured substantially in the United States," and RIGEL agrees to take all reasonable action necessary on its part as licensee to enable STANFORD to satisfy its obligation thereunder relating to Inventions.

5. DILIGENCE; PROGRESS REPORTS

5.1 As an inducement to STANFORD to enter into this Agreement, RIGEL agrees to use all commercially reasonable efforts and diligence to proceed with the development, manufacture and sale of Licensed Products and to diligently develop markets for the Licensed Products. RIGEL shall demonstrate such diligence to STANFORD by achieving the following goals:

(a) before the first anniversary of the Effective Date, RIGEL shall identify and characterize beta gal mutants with improved properties (e.g., mutants which have lower affinities than those disclosed in the Provisional and yet still provide adequate complementary binding characteristics such that the assay's signal to noise ratio is adequate for high throughput commercial use.)

(b) before the second anniversary of the Effective Date, RIGEL shall establish two (2) new high throughput screening assays that utilize the Licensed Technology, one (1) of which is primarily useful for target identification and one (1) of which is primarily useful for screening to identify small molecules that bind to drug targets; and

(c) before the fourth anniversary of the Effective Date, use the assays described in (b) to identify one new drug target and one small molecule that competes with the binding of molecules to a drug target.

5.2 If RIGEL is unable to demonstrate its diligence by achieving the goals provided in Section 5.1 within the time frames set forth therein, the parties shall meet no later than thirty (30) days after the relevant date set forth in Section 5.1 to discuss in good faith the reasons for such

failure, and mutually acceptable mechanisms for remedying such failure. If the parties do not agree upon modifications to the diligence requirements set forth in Section 5.1 during such discussion, then STANFORD may thereafter convert RIGEL's exclusive license under the Licensed Patents to non-exclusive upon thirty (30) days written notice to RIGEL.

5.3 If RIGEL succeeds in meeting the goals provided in Section 5.1, RIGEL and STANFORD agree to meet within ninety (90) days prior to the fourth anniversary of the Effective Date to establish further mutually acceptable diligence requirements applicable to the next two (2) year period during the term of the Agreement. If the parties, after good faith effort, cannot agree on such additional requirements, STANFORD may in its sole discretion elect to convert RIGEL's exclusive license under the Licensed Patents to non-exclusive as of the fourth anniversary of the Effective Date by written notice to RIGEL.

5.4 On or before August 1, 1998 and each anniversary thereof until RIGEL markets Licensed Products, RIGEL shall make a written annual report to STANFORD covering RIGEL's progress during the preceding year toward commercial use of Licensed Products. Such report shall include, as a minimum, information sufficient to enable STANFORD to satisfy reporting requirements of the U.S. Government and for STANFORD to ascertain progress by RIGEL toward meeting the diligence requirements of this Article 5.

6. PAYMENTS AND ROYALTIES

6.1 RIGEL shall upon the Effective Date:

(a) pay to STANFORD a noncreditable, nonrefundable license issue royalty of [text omitted in original signature document]; and

(b) issue to STANFORD [text omitted in original signature document] Stock pursuant to a stock purchase agreement to be separately executed by the parties.

6.2 Subject to Section 6.6, RIGEL also agrees to pay the following minimum annual royalties to STANFORD within thirty (30) days after the occurrence of each date below:

<TABLE>

<CAPTION>

Anniversary of Effective Date	Minimum Annual Royalty Due
<S>	<C>
First and Second	[text omitted in original signature document]
Third through Fifth	[text omitted in original signature document]
Sixth and Thereafter	[text omitted in original signature document]

</TABLE>

These minimum annual royalty payments are nonrefundable, but they are creditable against earned royalties due to Stanford pursuant to Section 6.4. In addition, the minimum annual royalties set forth in this Section 6.2 shall be reduced by fifty percent (50%) if STANFORD abandons all patent applications from which Licensed Patents could issue prior to the time that any Licensed Patents issue.

6.3 RIGEL also agrees to pay to STANFORD upon the occurrence of the following events, the following amounts:

<TABLE>
<CAPTION>

Event	Milestones
<S>	<C>
Earlier of the execution of the first sublicense by Rigel under the Licensed Technology or 18 months after the Effective Date	[text omitted in original signature document]
Earlier of the execution of the second sublicense by Rigel under the Licensed Technology or 48 months after the Effective Date	[text omitted in original signature document]
Earlier of the execution of the third sublicense by Rigel under the Licensed Technology or 78 months after the Effective Date	[text omitted in original signature document]
Execution of any additional sublicenses by Rigel after payment of all of the foregoing milestones	[text omitted in original signature document]

</TABLE>

6.4 RIGEL shall pay to STANFORD earned royalties of [text omitted in original signature document] of Net Sales during the Exclusivity Term. Should total earned royalties due on Licensed Products to STANFORD under this Agreement and any other agreement between STANFORD and RIGEL (the "Other Agreements") equal or exceed [text omitted in original signature document] of Net Sales, STANFORD shall, upon request by RIGEL, meet with RIGEL to discuss an appropriate mechanism, if RIGEL's royalty obligations under this Agreement and the Other Agreements render further development and commercialization of License Products uneconomic. The parties will discuss in good faith appropriate adjustments to RIGEL's obligations under this Agreement.

6.5 RIGEL shall also pay to STANFORD [text omitted in original signature document] upon the issuance of the first patent included in the Licensed Patents.

6.6 Within thirty (30) days after the license granted under the Licensed Patents pursuant to Section 3.1 becomes non-exclusive pursuant to Sections 3.3, 5.2 or 5.3, STANFORD shall provide to RIGEL a written summary of all non-confidential material terms of any other license agreements with third parties relating to the Licensed Technology. STANFORD shall use reasonable efforts to obtain consent of any such third parties to disclose such material terms or at least a general description of the economic terms of such other license agreements to RIGEL. Within thirty (30) days after receiving such summary, RIGEL shall elect one of the following options by written notice to STANFORD:

(a) to allow this Agreement to continue in full force and effect, except that the minimum annual royalties due to STANFORD pursuant to Section 6.2 shall be reduced by fifty percent (50%); or

(b) to modify the terms of this Agreement to include terms no less favorable to RIGEL than those STANFORD then provides to third party licensees of the Licensed Technology.

If no such license agreement between STANFORD and any such third party exists at the time RIGEL must elect either (a) or (b), then (a) shall automatically apply. If RIGEL elects the option set forth in Section 6.6(a), such a reduction shall be in addition to any reduction resulting from the application of Section 6.2. If RIGEL elects the option set forth in Section 6.6(b), RIGEL and STANFORD shall modify the Agreement to contain all rights and obligations contained in licenses available to such other licensees.

6.7 Creditable payments under this Agreement shall be offset against up to fifty percent (50%) of each earned royalty payment which RIGEL would be required to pay pursuant to Section 6.4, until the entire creditable amount is exhausted.

6.8 If this Agreement is not terminated in accordance with other provisions hereof, RIGEL's obligation to pay royalties hereunder shall continue until ten (10) years after first commercial sale of Licensed Products.

6.9 The royalty on sales in currencies other than U.S. Dollars shall be calculated using the appropriate foreign exchange rate for such currency quoted by the Bank of America (San Francisco) foreign exchange desk, on the close of business on the last banking day of each calendar quarter. Royalty payments to STANFORD shall be in U.S. Dollars. All non-U.S. taxes related to royalty payments shall be paid by RIGEL and are not deductible from the payments due STANFORD.

7. ROYALTY REPORTS, PAYMENTS, AND ACCOUNTING

7.1 QUARTERLY EARNED ROYALTY PAYMENT AND REPORT - Beginning with the first sale of Licensed Products, RIGEL shall make written reports (even if there are no sales) and earned royalty payments to STANFORD within thirty (30) days after the end of each calendar quarter. This report shall be in the form of the report of Appendix B and shall state the number, description and aggregate Net Sales of Licensed Products during such completed calendar quarter, and shall state the resulting calculation pursuant to Section 6.4 of earned royalty payments due STANFORD for such completed calendar quarter. Concurrent with the making of each such report, RIGEL shall include payment due STANFORD of royalties for the calendar quarter covered by such report.

7.2 ACCOUNTING - RIGEL agrees to keep and maintain records for a period of three (3) years showing the manufacture, sale, use and other disposition of products sold or otherwise disposed of under the licenses herein granted. Such records will include general ledger records showing cash receipts and expenses and records which include production records, customers, serial numbers and related information in sufficient detail to enable the royalties payable hereunder by RIGEL to be determined. RIGEL further agrees to permit its books and records to be examined by STANFORD from time to time to the extent necessary to verify reports provided

for in Section 7.1. Such examination is to be made by STANFORD or its designee, at the expense of STANFORD, except in the event that the results of the audit reveal an underreporting of royalties due STANFORD of five percent (5%) or more, then the audit costs shall be paid by RIGEL.

8. NEGATION OF WARRANTIES

8.1 Nothing in this Agreement is or shall be construed as:

(a) a warranty or representation by STANFORD as to the validity or scope of any Licensed Patents;

(b) a warranty or representation that anything made, used, sold or otherwise disposed of under any license granted in this Agreement is or will be free from infringement of patents, copyrights and other rights of third parties;

(c) an obligation to bring or prosecute actions or suits against third parties for infringement, except to the extent and in the circumstances described in Article 13;

(d) granting by implication, estoppel or otherwise any licenses or rights under patents or other rights of STANFORD or other persons other than Licensed Technology, regardless of whether such patents or other rights are dominant or subordinate to any Licensed Technology; or

(e) an obligation to furnish any technology or technological information other than the Licensed Technology.

8.2 Except as expressly set forth in this Agreement, STANFORD MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR

IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE LICENSED PRODUCT(S) WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER RIGHTS OR ANY OTHER EXPRESS OR IMPLIED WARRANTIES.

8.3 RIGEL agrees that nothing in this Agreement grants RIGEL any express or implied license or right under or to U.S. Patent 4,656,134 "Amplification of Eucaryotic Genes" or any patent application corresponding thereto.

9. INDEMNITY

9.1 LICENSEE agrees to indemnify, hold harmless, and defend STANFORD, UCSF-Stanford Health Care and Stanford Health Services and their respective trustees, officers, employees, students and agents against any and all claims for death, illness, personal injury, property damage, and improper business practices arising out of the manufacture, use, sale or

other disposition of Inventions, Licensed Products or Licensed Technology by RIGEL or RIGEL's sublicensee(s), or their customers.

9.2 STANFORD shall not be liable for any indirect, special, consequential or other damages whatsoever, whether grounded in tort (including negligence), strict liability, contract or otherwise. STANFORD shall not have any responsibilities or liabilities whatsoever with respect to Licensed Product(s).

9.3 LICENSEE shall at all times comply, through insurance or self-insurance, with all statutory workers' compensation and employers' liability requirements covering any and all employees with respect to activities performed under this Agreement.

9.4 In addition to the foregoing, LICENSEE shall maintain, during the term of this Agreement, Comprehensive General Liability Insurance, including Products Liability Insurance, with reputable and financially secure insurance carrier(s) to cover the activities of LICENSEE and its sublicensee(s). Such insurance shall provide minimum limits of liability of $5 Million and shall include STANFORD, UCSF-Stanford Health Care, Stanford Health Services, their trustees, directors, officers, employees, students and agents as additional insureds. Such insurance shall be written to cover claims incurred, discovered, manifested, or made during or after the expiration of this Agreement. At STANFORD's request, LICENSEE shall furnish a Certificate of Insurance evidencing primary coverage and requiring thirty (30) days prior written notice of cancellation or material change to STANFORD. LICENSEE shall advise STANFORD, in writing, that it maintains excess liability coverage (following form) over primary insurance for at least the minimum limits set forth above. All such insurance of LICENSEE shall be primary coverage; insurance of STANFORD, USCF-Stanford Health Care, and Stanford Health Services shall be excess and noncontributory.

10. MARKING

Prior to the issuance of patents on the Inventions, RIGEL agrees to mark Licensed Products (or their containers or labels) made, sold, or otherwise disposed of by it under the license granted in this Agreement with the words "Patent Pending," and following the issuance of one or more patents, with the numbers of the Licensed Patents.

11. STANFORD NAMES AND MARKS

RIGEL agrees not to identify STANFORD in any promotional advertising or other promotional materials to be disseminated to the public or any portion thereof or to use the name of any STANFORD faculty member, employee, or student or any trademark, service mark, trade name, or symbol of STANFORD, STANFORD Health Services or UC-Stanford Health Care, or that is associated with any of them, without STANFORD's prior written consent.

12. PATENT RIGHTS

12.1 STANFORD shall have the obligation to file, prosecute and maintain all patent applications and patents included in the Licensed Patents.

12.2 STANFORD will provide RIGEL with an opportunity to review and comment upon the prosecution strategy and to consult with STANFORD on the content of patent filings. In addition, STANFORD will provide RIGEL or a designee of RIGEL with copies of any correspondence relating to patent

applications and patents included in the Licensed Patents.

12.3 RIGEL shall have the right to designate, in its sole discretion, those foreign countries in which STANFORD will file, prosecute and maintain patents and patent applications included in the Licensed Patents. STANFORD may propose to file, prosecute and maintain Licensed Patents in a country which RIGEL has not designated pursuant to this Section 12.3. If RIGEL agrees to such designation, it shall reimburse STANFORD for the costs of such filing, prosecution and maintenance of such patents or patent applications pursuant to Section 12.4 and such patents or patent applications shall be included in the Licensed Patents. If RIGEL does not agree to such proposal, STANFORD may elect to proceed with such filing, prosecution or maintenance at its own expense, and such patents or patent applications in such country shall not be included in the Licensed Patents.

12.4 Within thirty (30) days after the Effective Date, RIGEL shall reimburse STANFORD for all costs incurred by STANFORD prior to the Effective Date in connection with the filing and prosecution of the patent applications described in Section 2.5 ("Prior Patent Costs"). RIGEL shall also reimburse STANFORD for all costs incurred by STANFORD after the Effective Date with respect to the filing, prosecution, issuance and maintenance of patent applications described in Section 2.5 and the Licensed Patents ("Future Patent Costs"); PROVIDED, HOWEVER, that:

(a) if STANFORD grants a license under the Licensed Patents to any third party (an "Other Licensee"), RIGEL's obligation to reimburse STANFORD under this Section 12.4(a) shall be reduced such that RIGEL and such Other Licensee(s) shall pay a pro-rata share of all Future Patent Costs incurred after the date STANFORD executes such license agreement with such Other Licensee (such pro-rata share shall be equal to the total Future Patent Costs incurred divided by the number of licensees under the Licensed Patents at the time such costs are incurred); and

(b) in addition to any reimbursement due RIGEL pursuant to Section 12.4(a), if STANFORD grants a license under the Licensed Patents to an Other Licensee prior to the second anniversary of the Effective Date, STANFORD shall reimburse RIGEL for fifty percent (50%) of the Prior Patent Costs.

13. INFRINGEMENT BY OTHERS: PROTECTION OF PATENTS

13.1 RIGEL shall promptly inform STANFORD of any suspected infringement of any Licensed Patents by a third party. During the Exclusivity Term, STANFORD and RIGEL each shall have the right to institute an action for infringement of the Licensed Patents against such third party in accordance with the following:

(a) if STANFORD and RIGEL agree to institute suit jointly, the suit shall be brought in both their names, the out-of-pocket costs thereof shall be borne equally, and any recovery or settlement shall be shared equally. RIGEL and STANFORD shall agree to the manner in which they shall exercise control over such action. STANFORD may, if it so desires, also be represented by separate counsel of its own selection, the fees for which counsel shall be paid by STANFORD;

(b) in the absence of agreement to institute a suit jointly, STANFORD may institute suit, and, at its option, join RIGEL as a plaintiff. If STANFORD decides to institute suit, then it shall notify RIGEL in writing. STANFORD shall bear the entire cost of such litigation and shall be entitled to retain the entire amount of any recovery or settlement; and

(c) in the absence of agreement to institute a suit jointly and if STANFORD notifies RIGEL that it has decided not to join in or institute a suit, as provided in (a) or (b) above, RIGEL may institute suit and, at its option, join STANFORD as a plaintiff. RIGEL shall bear the entire cost of such litigation. Any recovery in excess of litigation costs will be shared with STANFORD as follows:

(i) Any payment for past sales will be deemed to be Net Sales and RIGEL will pay STANFORD royalties thereon at the rates specified in Paragraph 6.4; and

(ii) any payment which covers future sales will be deemed a sublicense and royalties will be shared as specified in Paragraph 6.3 and Article 15.

LICENSEE and STANFORD agree to negotiate in good faith an appropriate compensation to STANFORD for any non-cash amounts or awards received in any settlement or cross-license resulting from a suit brought by RIGEL pursuant to this Section 13.1(c). STANFORD will not share in the portion of the recovery, if any, that is payment for "willful infringement."

13.2 Should either STANFORD or RIGEL commence a suit under the provisions of Section 13.1 and thereafter elect to abandon the same, it shall give timely notice to the other party who may, if it so desires, continue prosecution of such suit; PROVIDED, HOWEVER, that the sharing of expenses and any recovery in such suit shall be as agreed upon between STANFORD and RIGEL.

14. OTHER LICENSEE(S) OF STANFORD

14.1 If during the Exclusivity Term STANFORD discusses with, or has received an offer from, a third party (a "Potential Licensee") with respect to an opportunity for such Potential Licensee to obtain a license under the Licensed Technology within the Licensed Field of Use, STANFORD may so notify RIGEL. Such notice shall specify the field within which such Potential Licensee desires to obtain a license under the Licensed Technology (the "Field of Interest"). Within thirty (30) days after RIGEL receives a notice from STANFORD pursuant to this Section 14.1, the parties will meet to discuss RIGEL's current activities directed toward, or

plans for, developing Licensed Products useful within the Field of Interest. If RIGEL does not demonstrate that it is then diligently conducting such activities or provide plans for diligently developing Licensed Products within the Field of Interest that are reasonably acceptable to STANFORD, then RIGEL and STANFORD shall discuss in good faith reasonable modifications to the Agreement that exclude the Field of Interest from the definition of the Licensed Field of Use. STANFORD may thereafter license to such Potential Licensee the Licensed Technology in the Field of Interest.

14.2 If STANFORD has not entered into an agreement with a Service Provider outside the Licensed Field of Use during the Exclusivity Term, then after the expiration of the Exclusivity Term STANFORD and RIGEL agree to discuss in good faith how to modify appropriately the definition of the Licensed Field of Use to enable STANFORD to increase the interest of Service Providers in obtaining a license under the Licensed Technology outside any modified Licensed Field of Use.

15. SUBLICENSE(S)

15.1 RIGEL may grant sublicense(s) to its corporate partners in conjunction with a sublicense of RIGEL's proprietary technology other than the Licensed Technology and Improvements; provided that the Licensed Technology is applicable to the field within which RIGEL and such corporate partner are collaborating.

15.2 Any sublicense(s) granted by RIGEL under this Agreement shall be subject and subordinate to terms and conditions of this Agreement, except:

(a) Sublicense terms and conditions shall reflect that any sublicensee(s) shall not grant sublicenses to a third parties (subject to Section 15.4); and

(b) The earned royalty rate specified in the sublicense(s) may be at higher rates than the rates in this Agreement.

Any such sublicense(s) also shall expressly include the provisions of Articles 7, 8, and 9 for the benefit of STANFORD and provide for the transfer of all obligations, including the payment of royalties specified in such sublicense(s), to STANFORD or its designee, in the event that this Agreement is terminated if such sublicenses remain in effect after termination of this Agreement.

15.3 RIGEL agrees to provide STANFORD with a copy of any sublicense granted pursuant to this Article 15.

15.4 STANFORD agrees that RIGEL and/or its permitted sublicensee(s) may (i) distribute Licensed Products through their normal channels, and (ii) contract for the manufacture of Licensed Products with one or more third parties.

16. TERMINATION

16.1 RIGEL may terminate this Agreement by giving STANFORD notice in writing at least thirty (30) days in advance of the effective date of termination selected by RIGEL.

16.2 STANFORD may terminate this Agreement if RIGEL:

(a) is in default in payment of royalties or providing of reports;

(b) is in breach of any provision hereof (subject to Section 5.2); or

(c) intentionally provides any false report;

and fails to remedy any such default, breach, or false report within thirty (30) days after written notice thereof by STANFORD.

16.3 Surviving any termination are:

(a) RIGEL's obligation to pay royalties accrued or accruable;

(b) any cause of action or claim of RIGEL or STANFORD, accrued or to accrue, because of any breach or default by the other party; and

(c) the provisions of Sections 3.2, 3.5 and Articles 7, 8 and 9.

17. ASSIGNMENT

This Agreement may not be assigned by either party without the express written consent of the other party, except that RIGEL may assign the Agreement in connection with a merger, consolidation or sale of all or substantially all of RIGEL's assets.

18. ARBITRATION

18.1 Any controversy arising under or related to this Agreement, and any disputed claim by either party against the other under this Agreement excluding any dispute relating to patent validity or infringement arising under this Agreement, shall be settled by arbitration in accordance with the Licensing Agreement Arbitration Rules of the American Arbitration Association.

18.2 Upon request by either party, arbitration will be by a third party arbitrator mutually agreed upon in writing by RIGEL and STANFORD within thirty (30) days of such arbitration request. Judgement upon the award rendered by the arbitrator shall be final and nonappealable and may be entered in any court having jurisdiction thereof.

18.3 The parties shall be entitled to discovery in like manner as if the arbitration were a civil suit in the California Superior Court.

18.4 Any arbitration shall be held at Stanford, California, unless the parties hereto mutually agree in writing to another place.

19. NOTICES

All notices under this Agreement shall be deemed to have been fully given when done in writing and deposited in the United States mail, registered or certified, and addressed as follows:

To STANFORD: Office of Technology Licensing

STANFORD University
900 Welch Road, Suite 350
Palo Alto, CA 94304-1850

Attention: Director

To RIGEL: Rigel, Inc.
772 Lucerne Drive
Sunnyvale, CA 94086

Attention: President

Either party may change its address upon written notice to the other party.

20. WAIVER

None of the terms of this Agreement can be waived except by the written consent of the party waiving compliance.

21. APPLICABLE LAW

This Agreement shall be governed by the laws of the State of California

applicable to agreements negotiated, executed and performed wholly within California.

22. SEVERABILITY; ENTIRE AGREEMENT

If any provision of this Agreement shall be held to be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not be in any way affected or impaired thereby. This Agreement embodies the entire understanding of the parties and shall supersede all previous [text omitted in original signature document] communications, representations or understandings, either oral or written, between the parties relating to the subject matter hereof. No amendment or modification hereof shall be valid or binding upon the parties unless made in writing and signed by duly authorized representatives of both parties.

23. COUNTERPARTS

This Agreement may be executed in counterparts, each of which shall be deemed an original and all of which together shall constitute one legal instrument.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement in duplicate originals by their duly authorized officers or representatives.

THE BOARD OF TRUSTEES OF THE LELAND
STANFORD JUNIOR UNIVERSITY

Signature /s/ Katherine Ku

Name Katherine Ku

Title Director

Date April 15, 1998

RIGEL

Signature /s/ James M. Gower

Name James M. Gower

Title President & CEO

Date 3/27/98

EXHIBIT A
LICENSED BIOLOGICAL MATERIALS

[there was no text in Exhibit A]

EXHIBIT 10.7

COLLABORATIVE RESEARCH AND LICENSE AGREEMENT

THIS COLLABORATIVE RESEARCH AND LICENSE AGREEMENT ("the Agreement") is entered into as of January 31, 1999 ("Effective Date") by and between PFIZER INC, a Delaware corporation, having an office at 235 East 42nd Street, New York, New York 10017-5755 ("Pfizer") and RIGEL PHARMACEUTICALS, INC., a Delaware corporation, having an address at 772 Lucerne Drive, Sunnyvale, California 94086 ("Rigel"). Pfizer and Rigel and their Affiliates may be referred to herein individually as a "Party" or collectively as the "Parties."

WHEREAS, Rigel has the capability and expertise to undertake research for the discovery of novel and selective elements of the IL-4 signaling pathway involved in the modulation of IgE synthesis that are suitable targets for an IgE synthesis-inhibitor, lead identification program;

WHEREAS, Rigel owns the patents, patent applications and licenses with third parties set forth in Exhibit A attached to and made a part of this Agreement with respect to retroviral expression technology and cell lines engineered for identifying components of the IL-4 pathway; and

WHEREAS, Pfizer has the capability to undertake research for the discovery and evaluation of biosynthetic, biochemical and organic matter for treatment of disease and also the capability for clinical analysis, manufacturing and marketing with respect to a wide variety of drugs for medicinal use in human and animal health; and

WHEREAS, the Parties plan to seek patent protection for biological elements that regulate IgE synthesis which will serve as molecular targets for compounds from Pfizer's chemical library and patent protection for Licensed Products which make up the subject matter of this Agreement;

NOW, THEREFORE, the Parties agree as follows:

1. DEFINITIONS

Whenever used in this Agreement, the terms defined in this Section 1 shall have the meanings specified.

1.1 "AFFILIATE" means (a) any corporation or other legal entity owning, directly or indirectly, fifty percent (50%) or more of the voting capital shares or similar voting securities of a Party; (b) any corporation or other legal entity fifty percent (50%) or more of the voting capital shares or similar voting rights of which is owned, directly or indirectly, by a Party; or (c) any corporation or other legal entity fifty percent (50%) or more of the voting capital shares or similar voting rights of which is owned, directly or indirectly, by a corporation or other legal entity which owns, directly or indirectly, fifty percent (50%) or more of the voting capital shares or similar voting securities of such Party.

1.2 "ANIMAL HEALTH PRODUCT" shall mean any Licensed Product intended for animal patients.

1.3 "AREA" means research directed to the discovery of cDNA, peptides or proteins within the IL-4 signaling pathway that selectively regulate IgE synthesis further described in the Research Plan.

1.4 "DISCOVERY MILESTONE" shall have the meaning given to that term in Section 3.3.

1.5 "EFFECTIVE DATE" is January 31, 1999.

1.6 "HIGH THROUGHPUT SCREEN" or "HTS" means a primary assay performed by or under the direction of Pfizer that incorporates a Molecular Target for the purpose of identifying potential Licensed Products.

1.7 "HUMAN HEALTH PRODUCT" shall mean any Licensed Product intended for human patients.

1.8 "LICENSED PRODUCT" means any chemical or biological entity that (a) directly, selectively and specifically modulates the activity of a Molecular Target; (b) was identified by Pfizer in HTS; (c) is to be used for the management of any disease or any therapeutic indication in human or animal patients; and (d) the manufacture, use or sale of which would infringe Valid Claims.

1.9 "MOLECULAR TARGET" shall mean any cDNA, peptide or protein

identified in the Research Program.

1.10 "NET SALES" means the gross amount invoiced by Pfizer, its Affiliates, or any sublicensee of Pfizer for sales to a third party or third parties of Licensed Products, less normal and customary trade discounts actually allowed, rebates, returns, credits, taxes the legal incidence of which is on the purchaser and separately shown on Pfizer's or any sublicensee of Pfizer's invoices and transportation, insurance and postage charges, if prepaid by Pfizer or any sublicensee of Pfizer and billed on Pfizer's or any sublicensee of Pfizer's invoices as a separate item.

1.11 "PRODUCT PATENT RIGHTS" shall mean all the Valid Claims covering Licensed Products, whether domestic or foreign, including all continuations, continuations-in-part, divisions, and renewals, all letters patent granted thereon, and all reissues, re-examinations and extensions thereof.

1.12 "PFIZER COMPOUND LIBRARY" means those Pfizer compounds which it may use for HTS.

1.13 "PFIZER CONFIDENTIAL INFORMATION" means all information about any element of Pfizer Technology or Program Technology, except for Program Technology assigned to Rigel pursuant to Section 5.1, which is disclosed by Pfizer to Rigel and designated "Confidential" in writing by Pfizer at the time of disclosure or within thirty (30) days following disclosure to Rigel to the extent that such information as of the date of disclosure to Rigel is not (i) demonstrably known to Rigel other than by virtue of a prior confidential disclosure to Rigel by Pfizer; (ii) disclosed in published literature, or otherwise generally known to the public through no fault or omission of Rigel; or (iii) obtained from a third party free from any obligation of confidentiality to Pfizer prior to disclosure to Rigel by Pfizer.

1.14 "PFIZER TECHNOLOGY" means Technology that is or was developed by employees of or consultants to Pfizer alone or jointly with third parties prior to the Effective Date, but, in the case of consultants or third parties, only to the extent Pfizer has the right to grant rights to such Technology.

1.15 "PROGRAM INVENTIONS" shall have the meaning given to it in Section 5.1.

1.16 "PROGRAM TECHNOLOGY" means Technology within the Area that is or was developed by employees of or consultants to Pfizer or Rigel solely or jointly with each other in the course of performing the Research Program; PROVIDED, HOWEVER, that Rigel's peptide library, Phoenix cell line and Felix cell line shall not be Program Technology and are owned by or exclusively licensed to Rigel and deemed to be Rigel Technology and that the Pfizer Compound Library shall not be Program Technology and is owned by or exclusively licensed and deemed to be Pfizer Technology.

1.17 "RECOMMENDED FOR DEVELOPMENT NOTICE" or "RFD" shall have the meaning provided in the Research Plan.

1.18 "RESEARCH COMMITTEE" shall have the meaning given to that term in Section 2.5.1.

1.19 "RESEARCH PERIOD" means the period beginning on the Effective Date and ending on the date the Research Program terminates as provided in Section 8.1.

1.20 "RESEARCH PLAN" means the written plan describing the research and development to be carried out by Rigel and Pfizer pursuant to this Agreement, as amended from time to time. The initial Research Plan is appended to this Agreement as Exhibit B.

1.21 "RESEARCH PROGRAM" is the collaborative research program in the Area conducted by Pfizer and Rigel pursuant to the Research Plan.

1.22 "RIGEL CONFIDENTIAL INFORMATION" means all information about any element of the Rigel Technology or Program Technology, except for Program Technology assigned to Pfizer pursuant to Section 5.1, which is disclosed by Rigel to Pfizer and designated "Confidential" in writing by Rigel at the time of disclosure or within thirty (30) days following disclosure to Pfizer to the extent that such information as of the date of disclosure to Pfizer is not (i) demonstrably known to Pfizer other than by virtue of a prior confidential disclosure to Pfizer

by Rigel; (ii) disclosed in published literature, or otherwise generally known to the public through no fault or omission of Pfizer; or (iii) obtained from a third party free from any obligation of confidentiality to Rigel prior to disclosure to Pfizer by Rigel.

1.23 "RIGEL PATENT RIGHTS" shall mean the Valid Claims in Rigel's patents and patent applications, listed in Exhibit A, any patents granted thereon, including any divisions, continuations, continuations-in-part, renewals, extensions, reexaminations, reissues or foreign counterparts thereof.

1.24 "RIGEL TECHNOLOGY" means Technology that is or was developed by employees of or consultants to Rigel alone or jointly with, or licensed to Rigel from, third parties prior to the Effective Date, but, in the case of consultants or third parties, only to the extent Rigel has the right to grant rights to such Technology.

1.25 "TARGET PATENT RIGHTS" shall have the meaning given to it in Section 6.1.1.

1.26 "TECHNOLOGY" means and includes all unpatented materials, technology, technical information, know-how, expertise and trade secrets.

1.27 "VALID CLAIM" means a claim within a patent or patent application so long as such claim shall not have been disclaimed by the Parties or shall not have been held invalid in a final decision rendered by a tribunal of competent jurisdiction from which no appeal has been or can be taken.

2. COLLABORATIVE RESEARCH PROGRAM

2.1 PURPOSE. Rigel and Pfizer shall conduct the Research Program throughout the Research Period. The objective of the Research Program is to discover Molecular Targets and to discover and develop Licensed Products.

2.2 AMENDMENT TO RESEARCH PLAN. The Research Plan may be amended from time to time by unanimous agreement of the Research Committee. Exhibit B shall be revised as necessary to reflect each such amendment.

2.3 CONTINGENT LICENSE. If during the Research Period Rigel ceases to do business or is unable to perform its duties and obligations as set forth in the Research Plan, whether due to insolvency, bankruptcy or any other reason, Pfizer shall have a non-exclusive license in the Area under the Rigel Technology and under Rigel Patent Rights to carry out and complete the Research Plan.

2.4 EXCLUSIVITY. Rigel agrees, during the Research Period, not to conduct research itself or sponsor any other research, or engage in any research sponsored with any third party in the Area except pursuant to the Research Program.

2.5 RESEARCH COMMITTEE.

2.5.1 PURPOSE. Pfizer and Rigel shall establish a Research Committee (the "Research Committee"):

(a) to review and evaluate progress of the Research Program throughout the Research Period under the Research Plan;

(b) to prepare any amendments to the Research Plans;

(c) to coordinate and monitor publication of research results obtained from and the exchange of information and materials that relate to the Research Program (This function will survive the termination of Research Period for a period of three (3) years).

2.5.2 Membership. Within ten (10) days of the Effective Date each Party shall appoint, in its sole discretion, four (4) members to the Research Committee. Substitutes may be appointed at any time. The members initially shall be:

Pfizer Appointees:	Rigel Appointees:
1. Dr. Scott Kennedy	1. Dr. Donald Payan
2. Dr. Edward D. Pagani	2. Dr. David Ferrick
3. Dr. Phil Vickers	3. Dr. Jeremy Caldwell
4. Dr. John Watson	4. To be determined.

2.5.3 Co-Chairs. The Research Committee shall be chaired by two (2) chairpersons, one appointed by Rigel and the other by Pfizer. The Co-Chairs will have the responsibility to ensure that a Research Committee meeting agenda is distributed to the Research Committee prior to the meeting.

2.5.4 Meetings. The Research Committee shall meet in person at least quarterly, at places and on dates suggested by Pfizer and by Rigel in turn. The location of the first meeting of the Research Committee shall be at Pfizer's election. Representatives of Pfizer or Rigel or both, in addition to members of the Research Committee, may attend such meetings at the invitation of either Party.

2.5.5 Minutes. The Research Committee shall keep accurate minutes of its deliberations which record all proposed decisions and all actions recommended or taken. Drafts of the minutes shall be delivered to all Research Committee members within fifteen (15) business days after each meeting. The Party choosing the location of the meeting shall be responsible for the preparation and circulation of the draft minutes. Draft minutes shall be edited by the co-chairpersons and shall be issued in final form only with their approval and agreement.

2.5.6 Decisions. All decisions of the Research Committee shall be by the unanimous vote of its members.

2.5.7 Expenses. Pfizer and Rigel shall each bear all expenses, including reasonable travel, related to the participation of their designated members of the Research Committee, respectively.

2.6 REPORTS AND MATERIALS.

2.6.1 Reports. Pfizer and Rigel each shall furnish to the Research Committee:

(a) summary written reports within fifteen (15) days after the end of each three (3) month period during the Research Period, describing its progress under the Research Plan; and

(b) a comprehensive written report within thirty (30) days after the end of the Research Period, describing in detail the work accomplished by it under the Research Plan during and discussing and evaluating the results of such work.

2.6.2 Materials. Rigel shall provide the following Program Technology to Pfizer:

(a) all Molecular Targets identified in the course of the Research Program;

(b) all other Program Technology, including biological materials, which is: specific to a Molecular Target which has been delivered to Pfizer by Rigel pursuant to Section 2.6.2(a); necessary for Pfizer to perform its obligations under the Research Program; or necessary for Pfizer to perform HTS with delivered Molecular Targets;

PROVIDED, HOWEVER, that such Program Technology will not include the transfer of any portion of Rigel's peptide libraries or Rigel Technology to Pfizer or the transfer of the Pfizer compound library or any portion of it to Rigel. Rigel agrees to supply reasonable quantities of Molecular Targets and biological materials specific to such Molecular Targets to Pfizer for the performance of the Research Program; and Pfizer agrees to supply reasonable quantities of Molecular Targets to perform HTS; PROVIDED, HOWEVER, that if either Party needs quantities of such materials which quantities are larger than would otherwise be anticipated by the supplying Party, the Parties will meet and discuss in good faith appropriate compensation to the supplying Party for such supply.

2.6.3 Pfizer's Selection of Molecular Targets. Pfizer may, in its sole, unfettered discretion, select for HTS during the Research Program and the three (3) year period immediately following the Research Period, any Molecular Target identified in the Research Program. To prevent the reversion of a Molecular Target to Rigel pursuant to Section 2.6.5, Pfizer

must commence HTS on a Molecular Target within a period of two (2) years after its selection of such Molecular Target for HTS.

2.6.4 Exclusivity of Molecular Targets. Molecular Targets for which Pfizer has initiated HTS shall be exclusive to Pfizer and shall not be conveyed to a third party in any manner by Rigel.

2.6.5 Reversion to Rigel. The following shall become Rigel Technology, and Rigel shall have no obligations to Pfizer with respect to: Molecular Targets which are not selected pursuant to Section 2.6.3; and any Molecular Target for which Pfizer has failed to satisfy the due diligence obligations set forth in Section 2.6.3; PROVIDED, HOWEVER, that no Molecular Target for which Pfizer has initiated HTS shall revert to Rigel.

2.7 LABORATORY FACILITIES AND PERSONNEL. Pfizer and Rigel shall provide suitable laboratory facilities, equipment and personnel for the work to be done under the Research Program.

2.8 DILIGENT EFFORTS. Rigel and Pfizer each shall use reasonably diligent efforts to achieve the objectives of the Research Program.

2.9 KEY INVESTIGATOR. If during the Research Period Dr. Donald Payan's association with Rigel, in the capacity as chief scientific officer or a similar role ends for any reason and the Parties are unable to agree on a successor acceptable to Pfizer, in its sole and unfettered discretion, within one hundred eighty (180) days of his dissociation, Pfizer may terminate this Agreement pursuant to Section 8.3.1.

3. PAYMENTS.

3.1 RESEARCH PROGRAM FUNDING.

3.1.1 Pfizer will fund the research to be performed by Rigel, pursuant to the Agreement, according to the following schedule:

COMMITMENT YEAR	ANNUAL COMMITMENT
1	$2,350,000.00
2	$2,350,000.00

The funding payments of two million three hundred and fifty thousand dollars ($2,350,000.00) shall support the work of the equivalent of ten (10) full time employees ("FTEs") of Rigel.

3.1.2 All funding payments shall be made quarterly in advance for work scheduled to be performed by Rigel during any three (3) month period, against Rigel's invoice for the FTEs allocated to the Research Program for such three (3) month period. Adjustments as necessary to reflect the work actually performed by Rigel shall be made at the end of each three (3) month period and shall be reflected in Rigel's invoice for the next three (3) month period. It is understood that all payments pursuant to this Section are non-creditable and non-refundable. Rigel shall also furnish to Pfizer the name and percent effort of each Rigel employee assigned to perform the Research Plan during each three (3) month period.

3.1.3 The amount of the funding payment for each quarter shall be based on the work in progress pursuant to the applicable Research Plan and the associated annual budget for Research Program personnel (FTEs); provided, however, that the aggregate amount of funding payments made in any commitment year shall not exceed the annual commitment for such commitment year.

3.1.4 Rigel shall keep for three (3) years from the conclusion of the Research Period complete and accurate records of its expenditures of payments received by it pursuant to

this Research Agreement. The records shall conform to generally accepted accounting practices (GAAP) as applied to similar companies similarly situated. Pfizer shall have the right at its own expense during the Research Period and during the subsequent three-year period to appoint an independent

certified public accountant reasonably acceptable to Rigel to inspect said records to verify the accuracy of the FTE allocation, pursuant to the Research Plan. Upon reasonable notice by Pfizer, Rigel shall make its records available for inspection by the independent certified public accountant during regular business hours at the place or places where such records are customarily kept, to verify the accuracy of the FTE allocation. This right of inspection shall not be exercised more than once in any calendar year and not more than once with respect to records covering any specific period of time. All information concerning such expenditures, and all information learned in the course of any audit or inspection, shall be deemed to be Rigel's Confidential Information. The failure of Pfizer to request verification of any expenditures before or during the three-year period shall be considered acceptance by Pfizer of the accuracy of such FTE allocation, and Rigel shall have no obligation to maintain any records pertaining to such report or statement beyond such three year period. The results of such inspection, if any, shall be binding on the parties.

3.1.5 If Pfizer, in its sole, unfettered discretion, extends the Research Program for a third year as set forth in Section 8.4, Pfizer shall pay Rigel two million five hundred thousand dollars ($2,500,000.00) with respect to the extension period on the same terms and conditions set forth in this Section 3. The funding payments shall support the work of ten (10) Rigel FTEs.

3.2 INITIAL PAYMENT. Within fifteen (15) days of the execution of this Agreement, Pfizer will pay to Rigel a one time, non refundable, noncreditable payment of two million dollars ($2,000,000.00).

3.3 DISCOVERY MILESTONE PAYMENTS. Within sixty (60) days after Rigel's delivery to Pfizer of Molecular Targets meeting the D3/D4 criteria set forth in Exhibit B and within thirty (30) days after Pfizer's selection, in its sole, unfettered discretion, of a Molecular Target for HTS ("Discovery Milestones"), as the case may be, Pfizer shall pay Rigel according to the following schedule:

DISCOVERY STAGE	DELIVERABLE	MILESTONE PAYMENT
D3	Molecular Targets No. 1-3	$75,000.00 each
D3	Molecular Targets No. 4-6	$100,000.00 each
D3	Molecular Targets No. 7+	$150,000.00 each
D4a/D4b	Molecular Targets No.1-3	$150,000.00 each
D4a/D4b	Molecular Targets No.4-6	$200,000.00 each
D4a/D4b	Molecular Targets No.7+	$250,000.00 each
HTS	Molecular Target No.1	$200,000.00

HTS	Molecular Target No.2	$250,000.00
HTS	Molecular Target No.3	$300,000.00
HTS	Molecular Target No.4	$350,000.00
HTS	Molecular Target No.5	$400,000.00
HTS	Molecular Target No.6	$450,000.00
HTS	Molecular Target No.7+	No Additional Payments

3.4 DISCOVERY MILESTONE PAYMENT CHARACTERISTICS. Discovery Milestone payments are in addition to the other payments in this Section 3 and are noncreditable and non-refundable. If Pfizer in its sole, unfettered discretion, selects a Molecular Target for HTS which does not meet the criteria for D3 or D4, such Molecular Target shall be deemed to have met both D3 and D4 criteria for the purposes of the payment for Discovery Milestones to Rigel under Section 3.3.

3.5 LIMITATION OF DISCOVERY MILESTONE PAYMENTS. Irrespective of the number of Molecular Targets meeting the criteria or the number of Molecular Targets selected by Pfizer for HTS, the aggregate amount which Pfizer shall pay to Rigel for Discovery Milestones shall not exceed (a) one million three hundred fifty thousand dollars ($1,350,000.00) in the case of Molecular Targets meeting the D3 criteria; (b) one million eight hundred thousand dollars ($1,800,000.00) in the case of Molecular Targets which meet the

D4a/D4b criteria; and (c) one million nine hundred fifty thousand dollars ($1,950,000.00) in the case of Molecular Targets selected for HTS in Pfizer's sole, unfettered discretion.

3.6 RECOMMENDED FOR DEVELOPMENT. Pfizer will pay to Rigel the sum of five hundred thousand dollars ($500,000.00) each time Pfizer issues a Recommended for Development Notice for a Human Health Product and a sum of two hundred fifty thousand dollars ($250,000.00) each time Pfizer issues a RFD notice for a Animal Health Product; PROVIDED, HOWEVER, that such payment will be made only once for each compound identified in a specific Pfizer HTS for a specific indication and will not include back-up compounds identified in the same HTS for the same indication. These payments are noncreditable and non-refundable, and shall be paid to Rigel within thirty (30) days of Pfizer's issuance of the applicable RFD notice.

3.7 ROYALTIES ON NET SALES OF LICENSED PRODUCTS.

3.7.1 Pfizer shall pay Rigel a royalty based on the Net Sales of each Licensed Product. Such royalty shall be paid with respect to each country of the world from the date of the first commercial sale (the date of the invoice of Pfizer or any sublicensee of Pfizer with respect to such sale) of such Licensed Product in each such country until the expiration of the last Product Patent Right to expire with respect to each such country and each such Licensed Product. If the manufacture and sale of a Licensed Product takes place in countries where there are no Product Patent Rights, Pfizer will pay to Rigel a royalty based on the Net Sales of each Licensed Product in each such country for ten (10) years after the first commercial sale of such Licensed Product in such country.

3.7.2 Unpatented Products. Pfizer will commercialize only those products derived or resulting from HTS which are covered by Product Patent Rights. If, in the unlikely

event, Pfizer determines in its absolute, unfettered discretion to commercialize an unpatented product, it will meet with Rigel to discuss additional compensation, if any, to Rigel, for use of the Molecular Target on the basis of which Pfizer conducted HTS to identify such product given Pfizer's advancement and commercialization of an unpatented product will have involved extraordinary development costs to Pfizer.

3.8 ROYALTY RATES. The royalty paid each year shall be based on increments of world-wide Net Sales with respect to each of the Licensed Products according to the following schedule:

<TABLE>
<CAPTION>

	HUMAN HEALTH PRODUCT	ANIMAL HEALTH PRODUCT
Annual Net Sales (Dollars)	Royalty Rate	Royalty Rate
<S>	<C>	<C>
$0-$500MM	2%	1%
> $500MM < $750MM	--	2%
> $500MM < 1B	3%	--
> = $750MM	--	3%
> = $1B	4%	--

</TABLE>

3.9 PAYMENT DATES FOR ROYALTIES. Royalties shall be paid by Pfizer on Net Sales within sixty (60) days after the end of each calendar quarter in which such Net Sales are made. Such payments shall be accompanied by a statement showing the Net Sales of each Licensed Product by Pfizer or any sublicensee of Pfizer in each country, the applicable royalty rate for such Licensed Product, and a calculation of the amount of royalty due, including any offsets.

3.10 ACCOUNTING FOR ROYALTIES. The Net Sales used for computing the royalties payable to Rigel by Pfizer shall be computed in U.S. dollars, and royalties shall be paid in U.S. dollars by wire transfer in immediately available funds to a U.S. account designated by Rigel, or by other mutually acceptable means. For purposes of determining the amount of royalties due, the

amount of Net Sales in any foreign currency shall be computed by (a) converting such amount into U.S. dollars at the prevailing commercial rate of exchange for purchasing dollars with such foreign currency as published in the Wall Street Journal for the close of the last business day of the calendar quarter for which the relevant royalty payment is to be made by Pfizer; and (b) deducting the amount of any governmental tax, duty, charge, or other fee actually paid in respect of such conversion into, and remittance of U.S. dollars.

3.11 RECORDS FOR ROYALTIES. Pfizer shall keep for three (3) years from the date of each payment of royalties complete and accurate records of sales by Pfizer, its Affiliates or sublicensees of each Licensed Product in sufficient detail to allow the accruing royalties to be determined accurately. Rigel shall have the right for a period of three (3) years after receiving any report or statement with respect to royalties due and payable to appoint at its expense (except as otherwise provided in this Section 3.11), an independent certified public accountant reasonably acceptable to Pfizer to inspect the relevant records of Pfizer, its Affiliates or

sublicensees to verify such report or statement. Pfizer, its Affiliates or sublicensees shall make its records available for inspection by such independent certified public accountant during regular business hours at such place or places where such records are customarily kept, upon reasonable notice from Rigel, to verify the accuracy of the reports and payments. Such inspection right shall not be exercised more than once in any calendar year nor more than once with respect to sales in any given period. Rigel agrees to hold in strict confidence all information concerning royalty payments and reports, and all information learned in the course of any audit or inspection, except to the extent necessary for Rigel to reveal such information in order to enforce its rights under this Agreement or if disclosure is required by law. The failure of Rigel to request verification of any report or statement during said three (3) year period shall be considered acceptance of the accuracy of such report, and Pfizer shall have no obligation to maintain records pertaining to such report or statement beyond said three (3) year period. The findings of each inspection, if any, shall be binding on both Parties.

3.12 MILESTONE PAYMENTS FOR LICENSED PRODUCTS. Pfizer shall pay Rigel, within sixty (60) days of the completion of each event set forth below ("Event"), the payment listed opposite that Event. Payments shall be made in U.S. dollars by wire transfer in immediately available funds to a U.S. bank account designated by Rigel, or other mutually acceptable means. Pfizer shall be obligated to make each payment only once with respect to each Licensed Product affected by an Event and such payment for such Event shall not be due with respect to any subsequent Licensed Product directed to a Molecular Target and indication which has previously been the subject of the same Event. With the exception of any such milestone paid to Rigel for the occurrence of the earlier of Submission of IND or initiation of human (Section 3.12.1(i)) or animal (Section 3.12.2(i)) clinical trials, payments made by Pfizer pursuant to this Section 3.12 with respect to a Licensed Product shall be credited against sums due to Rigel pursuant to Section 3.8 of this Agreement with respect to Net Sales of such Licensed Product. Fifty percent (50%) of the milestone payment paid to Rigel for commencement of Phase III human clinical trials (Section 3.12.1(ii)) and submission of NADA for animal use (Section 3.12.2 (ii)) shall be credited against royalty payments and one hundred percent (100%) of milestone payments paid to Rigel for NDA/PLA filing for human use (Section 3.12.1 (iii)) and for NADA/PLA approval in any country for animal use (Section 3.12.2 (iii)); PROVIDED, HOWEVER, that the sums due pursuant to Section 3.8 in any calendar year with respect to such Licensed Product shall not be reduced by virtue of this credit by more than fifty percent (50%):

3.12.1 HUMAN HEALTH PRODUCT

<TABLE>
<CAPTION>

EVENT	AMOUNT (DOLLARS)
<S>	<C>
(i) Submission of INDA or initiation of human clinical testing in any country (whichever occurs first)	$1,000,000.00
(ii) Commencement of Phase III human clinical trials in any country	$2,000,000.00
(iii) NDA/PLA Filing in any country for human use	$4,000,000.00

</TABLE>

3.12.2 ANIMAL HEALTH PRODUCT

<TABLE>
<CAPTION>

EVENT	AMOUNT (DOLLARS)
<S>	<C>
(i) Submission of INAD or initiation of animal clinical testing in any country (whichever occurs first)	$ 500,000.00
(ii) Submission of NADA in any country for animal use	$1,000,000.00
(iii) NADA/PLA Approval in any country for animal use	$2,000,000.00

</TABLE>

For the purposes of the foregoing, "IND" "INAD" or "INDA" shall mean an Investigational New Drug Application filed with the U.S. Food and Drug Administration (FDA), or a similar filing made with a counterpart health regulatory authority in another country; "NDA/PLA" or "NADA/PLA" shall mean a New Drug Application, Product License Application, or other application for authority to market a Licensed Product filed with the U.S. FDA or a counterpart health regulatory agency in another country.

3.13 U.S. FUNDS. Each payment pursuant to this Agreement shall be paid by Pfizer in U.S. currency by wire transfer in immediately available funds to an account designated by Rigel, or by other mutually acceptable means. If a payment due date is not otherwise specified in this Agreement, payment shall be made within thirty (30) days after receipt and acceptance by Pfizer of the invoice from Rigel.

4. TREATMENT OF CONFIDENTIAL INFORMATION

4.1 CONFIDENTIALITY

4.1.1 Pfizer and Rigel each recognize that the other's Confidential Information constitutes highly valuable, confidential information. Subject to the terms and conditions of the Agreement, Pfizer and Rigel each agree that during the Research Period and for five (5) years thereafter, it will keep confidential, and will cause its Affiliates to keep confidential, all Rigel Confidential Information or Pfizer Confidential Information, as the case may be, that is disclosed to it, or to any of its Affiliates pursuant to this Agreement. Neither Pfizer nor Rigel nor any of their respective Affiliates shall use such Confidential Information except as expressly permitted in this Agreement.

4.1.2 Pfizer and Rigel each agree that any disclosure of the other's Confidential Information to any officer, employee or agent of the other Party or of any of its Affiliates shall be made only if and to the extent necessary to carry out its responsibilities under this Agreement and shall be limited to the maximum extent possible consistent with such responsibilities. Pfizer and Rigel each agree not to disclose the other's Confidential Information to any third parties under any circumstance without written permission from the other Party. Each Party shall take such action, and shall cause its Affiliates to take such action, to preserve the confidentiality of each other's Confidential Information as it would customarily take to preserve the confidentiality of its own similar Confidential Information. Each Party, upon the other's request, will return all

the Confidential Information disclosed to the other Party pursuant to this Agreement, including all copies and extracts of documents, within sixty (60) days of the request upon the termination of this Agreement except for one (1) copy which may be kept for the purpose of complying with continuing obligations under this Agreement.

4.1.3 Rigel and Pfizer each represent that all of its employees, Affiliates and any consultants to such Party, participating in the Research Program who shall have access to Pfizer Technology, Rigel Technology or Program Technology and Pfizer Confidential Information and Rigel Confidential Information are bound by agreement to maintain such information in confidence with the same degree of care each Party holds it own confidential information.

4.2 PUBLICATION. Notwithstanding any matter set forth with particularity in this Agreement to the contrary, results obtained in the course of the Research Program may be submitted for publication following scientific review by the Research Committee and subsequent approval by Rigel's and Pfizer's

managements, which approval shall not be unreasonably withheld. After receipt of the proposed publication by both Pfizer's and Rigel's managements, written approval or disapproval shall be provided within thirty (30) days for a manuscript, within fourteen (14) days for an abstract for presentation at, or inclusion in the proceedings of a scientific meeting, and within fourteen (14) days for a transcript of an oral presentation to be given at a scientific meeting.

4.3 PUBLICITY. Except as required by law, and except for approved press releases which may be issued by each Party upon the signing of this Agreement, neither Party may disclose the terms of this Agreement without the prior written consent of the other Party; PROVIDED, HOWEVER, that Rigel may disclose the terms, or provide copies, of this Agreement as necessary in the normal course of business to bankers, investors and others bound by obligations of confidentiality not to disclose such information to other third parties in order to obtain financing.

4.4 PERMITTED DISCLOSURE.

4.4.1 If either Party is requested to disclose the Confidential Information in connection with a legal or administrative proceeding or is otherwise required by law to disclose the Confidential Information, such Party will give the other Party prompt notice of such request. The disclosing Party may seek an appropriate protective order or other remedy or waive compliance with the provisions of this Agreement. If such Party seeks a protective order or other remedy, the other Party will cooperate. If such Party fails to obtain a protective order or waive compliance with the relevant provisions of this Agreement, the other Party will disclose only that portion of Confidential Information which its legal counsel determines it is required to disclose.

4.4.2 Disclosure of Inventions. Each Party shall promptly inform the other about all inventions in the Area that are conceived, made or developed in the course of carrying out the Research Program by employees of, or consultants to, either of them solely, or jointly with employees of, or consultants to the other.

5. INTELLECTUAL PROPERTY RIGHTS.

5.1 OWNERSHIP. All Rigel Confidential Information, Rigel Technology and Rigel Patent Rights shall be owned by Rigel. All Pfizer Confidential Information, Pfizer Technology and Pfizer Patent Rights shall be owned by Pfizer. Program Technology (including, without limitation, any patentable invention or discovery) acquired, developed or made solely or jointly by employees or agents of either Party during the course of the Research Program ("Program Inventions") shall be the property of Pfizer and deemed to be Pfizer Confidential Information if it pertains to or is an improvement upon its HTS compound library or a Licensed Product and shall be the property of Rigel and deemed to be Rigel Confidential Information if it pertains to or is an improvement upon Rigel Patents, Rigel Technology or pertains to or is an improvement upon Molecular Targets which are not selected for HTS by Pfizer. Each Party shall cooperate with the other in completing any patent applications relating to Program Inventions, and in executing and delivering any instrument required to assign, convey or transfer to such other Party its interest, as provided in the preceding sentence.

5.2 GRANTS OF RESEARCH LICENSES.

5.2.1 Program License. Rigel and Pfizer each grants to the other a nonexclusive, worldwide, royalty-free license during the Research Period, including the right to grant sublicenses to Affiliates, to make and use Confidential Information, Program Technology and Product Patent Rights for the purpose of performing the Research Program; provided, however, that the other Party shall not acquire, by virtue of this Section or any other Section, any rights in the following:

(a) Rigel's peptide libraries;

(b) the Pfizer Compound Library; or

(c) any compounds active in the HTS which Pfizer chooses, in its sole, unfettered discretion, not to develop or otherwise include in Program Technology.

5.2.2 Research License.

(a) Rigel grants Pfizer an irrevocable, nonexclusive, worldwide license under its interest in Program Technology, except Rigel Core Technology, and under all intangible technology, technical information, know-how, expertise and trade secrets within Rigel Technology disclosed to Pfizer during the course of the Research Program, solely for the purpose of conducting research.

(b) Pfizer grants Rigel an irrevocable, nonexclusive, worldwide license under Pfizer's interest in all intangible technology, technical information, know-how, expertise and trade secrets within Program Technology, and under all intangible technology, technical information, know-how, expertise and trade secrets within Pfizer Technology disclosed to Rigel during the course of the Research Program, solely for the purpose of conducting research.

(c) For purposes of this Section 5.2.2, Rigel Core Technology shall mean:

(i) Rigel's peptide libraries

(ii) Rigel's Phoenix cell lines

(iii) Felix cell lines

5.3 GRANT OF COMMERCIALIZATION LICENSE, TERM, RIGHTS AND OBLIGATIONS.

5.3.1 Grant to Pfizer. Rigel hereby grants to Pfizer an exclusive, world-wide license, including the right to grant sublicenses, to research, manufacture, use, sell, offer for sale and import Licensed Products under Rigel's interest in the Product Patent Rights and the Molecular Targets.

5.3.2 Term of License. The term of the grant to Pfizer set forth in Section 5.3.1 shall begin on the Effective Date. The duration of the term of the grant shall be determined on a country-by-country basis. For any country in which there are Product Patent Rights, the term shall end on the date of the last to expire of the Product Patent Rights in such country. For all other countries, the term shall expire on the tenth (10th) anniversary of the first commercial sale of such Licensed Product in such country.

5.3.3 Paid-Up License. Upon the expiration of Pfizer's obligation to pay royalties on Net Sales of Licensed Products as provided in Section 3.7.1, the license granted in Section 5.3.1 shall become an irrevocable, nonexclusive paid-up license.

5.3.4 Pfizer Obligations.

(a) Pfizer shall use reasonably diligent efforts to exploit Licensed Products commercially employing similar effort to that applied to other products similarly situated; provided, however, Pfizer may, in its sole, unfettered judgement, discontinue the development or sale of any Licensed Product in any country in the world or all of them.

(b) If Pfizer grants a sublicense pursuant to this Section 5, Pfizer shall guarantee that any sublicensee fulfills all of Pfizer's obligations under this Agreement; PROVIDED, HOWEVER, that Pfizer shall not be relieved of its obligations pursuant to this Agreement.

5.3.5 Technical Assistance. Rigel shall provide to Pfizer or any sublicensee of Pfizer, at Pfizer's request and expense, any agreed technical assistance reasonably necessary to enable Pfizer or such sublicensee to manufacture, use, sell, offer for sale or import each Licensed Product and to enjoy fully all the rights granted to Pfizer pursuant to this License Agreement; provided, however, that Rigel is reasonably capable of providing that assistance. Pfizer shall reimburse Rigel's costs of providing such assistance.

6. PROVISIONS CONCERNING THE FILING, PROSECUTION AND MAINTENANCE OF PATENT RIGHTS.

The following provisions relate to the filing, prosecution and maintenance of patents and patent applications during the term of this Agreement:

6.1 FILING, PROSECUTION AND MAINTENANCE BY RIGEL.

6.1.1 With respect to any Rigel interest in patents and patent applications which claim a Molecular Target ("Target Patent Rights"), Rigel shall have the obligation:

(a) to file applications for letters patent on any invention included in Target Patent Rights; PROVIDED, HOWEVER, that Rigel shall consult with Pfizer regarding countries in which such patent applications should be filed and shall file patent applications in those countries where Pfizer requests that Rigel file such applications; and, further provided, that Rigel, at its option and expense, may file in countries where Pfizer does not request

that Rigel file such applications;

(b) to take all reasonable steps to prosecute all pending and new patent applications included within Target Patent Rights;

(c) to respond to oppositions, nullity actions, re-examinations, revocation actions and similar proceedings filed by third parties against the grant of letters patent for such applications;

(d) to maintain in force any letters patent included in Target Patent Rights by duly filing all necessary papers and paying any fees required by the patent laws of the particular country in which such letters patent were granted; and

(e) to cooperate fully with, and take all reasonable and necessary actions requested by, Pfizer in connection with the preparation, prosecution and maintenance of any letters patent included in Target Patent Rights.

Rigel shall notify Pfizer in a timely manner of any decision to abandon a pending patent application or an issued patent included in Target Patent Rights. Thereafter, Pfizer shall have the option, at its expense, of continuing to prosecute any such pending patent application or of keeping the issued patent in force.

6.1.2 Copies of Documents. Rigel shall provide to Pfizer copies of all patent applications that are part of Target Patent Rights prior to filing, for the purpose of obtaining substantive comment of Pfizer patent counsel. Rigel shall also provide to Pfizer copies of all documents relating to prosecution of all such patent applications in a timely manner and shall provide to Pfizer every six (6) months a report detailing their status.

6.1.3 Reimbursement of Costs for Filing Prosecuting and Maintaining Target Patent Rights. Within ninety (90) days of rendered patent services and thirty (30) days of receipt of invoices from Rigel, Pfizer shall reimburse Rigel for all the costs of writing, filing, prosecuting, responding to opposition and maintaining patent applications and patents in countries where Pfizer requests that patent applications be filed, prosecuted and maintained. Such reimbursement shall be in addition to payments described in Section 3. However, Pfizer may, upon sixty (60) days notice, request that Rigel discontinue filing or prosecution of patent applications in any country and discontinue reimbursing Rigel for the costs of filing, prosecuting, responding to opposition or maintaining such patent application or patent in any country. Rigel shall pay all costs in those countries in which Pfizer does not request that Rigel file, prosecute or maintain patent applications and patents, but in which Rigel, at its option, elects to do so.

6.1.4 Pfizer shall have the right to file on behalf of and as an agent for Rigel all applications and take all actions necessary to obtain patent extensions pursuant to 35 USC Section 156 and foreign counterparts for Target Patent Rights described in Section 6.1 licensed to Pfizer. Rigel agrees, to sign, at Pfizer's expense, such further documents and take such further actions as may be requested by Pfizer in this regard.

6.2 FILING, PROSECUTION AND MAINTENANCE BY PFIZER. With respect to Product Patent Rights claiming compounds in the Pfizer Compound Library or Licensed Products, Pfizer shall have those rights and duties ascribed to Rigel in Section 6.1, except that Pfizer will bear all related expenses.

6.3 DISCLAIMING A VALID CLAIM. Neither Party may disclaim a Valid Claim within Target Patent Rights or Product Patent Rights without the consent of the other.

6.4 ACTUAL OR THREATENED DISCLOSURE OR INFRINGEMENT. When information comes to the attention of Pfizer to the effect that any Target Patent Rights or Product Patent Rights relating to a Licensed Product have been or are threatened to be unlawfully infringed, Pfizer shall have the right at its expense to take such action as it may deem necessary to prosecute or prevent such unlawful infringement, including the right to bring or defend any suit, action or proceeding involving any such infringement. Pfizer shall notify Rigel promptly of the receipt of any such information and of the commencement of any such suit, action or proceeding. If Pfizer determines that it is necessary or desirable for Rigel to join any such suit, action or proceeding, Rigel shall, at Pfizer's expense, execute all papers and perform such other acts as may be reasonably required to permit Pfizer to commence such action, suit or proceeding in which case Pfizer shall hold Rigel free, clear and harmless from any and all costs and expenses of litigation, including attorneys fees. If Pfizer brings a suit, it shall have the right first to reimburse itself out of any sums recovered in such suit or in its settlement for all costs and expenses, including attorney's fees, related to such suit or settlement, and twenty percent (20%) of any funds that shall remain from said recovery shall be paid to Rigel and the balance of such

funds shall be retained by Pfizer. Each Party shall always have the right to be represented by counsel of its own selection and at its own expense in any suit instituted by the other for infringement under the terms of this Section. If Pfizer lacks standing and Rigel has standing to bring any such suit, action or proceeding, then Rigel shall do so at the request of Pfizer and at Pfizer's expense.

6.5 DEFENSE OF INFRINGEMENT CLAIMS. Rigel will cooperate with Pfizer at Pfizer's expense in the defense of any suit, action or proceeding against Pfizer or any sublicensee of Pfizer alleging the infringement of the intellectual property rights of a third party by reason of the use of Target Patent Rights or Product Patent Rights in the manufacture, use or sale of the Licensed Product. Pfizer shall give Rigel prompt written notice of the commencement of any such suit, action or proceeding or claim of infringement and will furnish Rigel a copy of each communication relating to the alleged infringement. Rigel shall give to Pfizer all authority (including the right to exclusive control of the defense of any such suit, action or proceeding and the exclusive right after consultation with Rigel, to compromise, litigate, settle or otherwise dispose of any such suit, action or proceeding), at Pfizer's expense, including by providing information and assistance necessary to defend or settle any such suit, action or proceeding; PROVIDED, HOWEVER, Pfizer shall obtain Rigel's prior consent to such part of any settlement which contemplates payment or other action by Rigel or has a material adverse effect on Rigel's

business. If the Parties agree that Rigel should institute or join any suit, action or proceeding pursuant to this Section, Pfizer may, at Pfizer's expense, join Rigel as a defendant if necessary or desirable, and Rigel shall execute all documents and take all other actions, including giving testimony, which may reasonably be required in connection with the prosecution of such suit, action or proceeding.

7. ACQUISITION OF RIGHTS FROM THIRD PARTIES. During the Research Period, each Party which acquires technology, patents or information in the Area from third parties during the course of the Research Program and wants to use such technology, patents or information in its performance of the Research Program shall obtain the prior written consent of the other Party, such consent not to be unreasonably withheld, prior to using such technology, patents or information in its performance of the Research Program. If the other Party gives the acquiring Party consent to use such third party technology, patents or information in the performance of the Research Program, such technology, patents or information shall be deemed either the Confidential Information or the Technology of the acquiring Party, as appropriate.

8. TERM, TERMINATION AND RENEWAL.

8.1 TERM. Unless sooner terminated or extended, the Research Period shall expire two (2) calendar years from the Effective Date. Unless sooner terminated or extended, the Agreement shall expire upon the expiration of Pfizer's financial obligations under this Agreement.

8.2 EVENTS OF TERMINATION. The following events shall constitute an event of termination ("Events of Termination"):

8.2.1 Rigel or Pfizer shall fail in any material respect to perform or observe any term, covenant or understanding contained in this Agreement, and any such failure shall remain unremedied for sixty (60) days after written notice to the failing Party; or

8.2.2 If any written representation or warranty by Rigel or Pfizer, or any of its officers, made under or in connection with this Agreement or any other contemporaneous written agreement between the Parties shall prove to have been incorrect in any material respect when made.

8.3 TERMINATION.

8.3.1 Upon the occurrence of any Event of Termination, the Party not responsible may, by written notice to the other Party, terminate this Agreement.

8.3.2 If Pfizer terminates this Agreement pursuant to Section 8.3.1, the terms and conditions of the Agreement, shall not terminate, but instead shall terminate or expire according to its terms. If Rigel terminates this Agreement pursuant to Section 8.3.1, the terms and conditions of the Agreement shall terminate immediately.

8.3.3 Termination of this Agreement for any reason, with or without cause, will not terminate the license granted pursuant to Section 5.2.2.

8.3.4 Termination of this Agreement for any reason shall be without prejudice to:

(a) the rights and obligations of the Parties in any Section which provide by its terms for performance by either Party subsequent to termination;

(b) Rigel's right to receive all royalty, milestone or other payments accrued hereunder; or

(c) any other remedies which either Party may otherwise have.

8.4 RENEWAL. Pfizer shall have the option, in its sole, unfettered discretion, of renewing the Research Program for a one (1) year extension period on the same terms and conditions set forth in this Agreement by written notice to Rigel. This option shall expire if not exercised by Pfizer at least three (3) months prior to the termination date described in Section 8.1. If Pfizer exercises this option, the Parties shall adopt an annual Research Plan during the ensuing ninety (90) day period, including a budget. All other terms and conditions of this Agreement shall otherwise remain in full force and effect except as set forth in Section 3.1.5.

9. REPRESENTATIONS AND WARRANTIES.

9.1 REPRESENTATIONS AND WARRANTIES OF BOTH PARTIES. Rigel and Pfizer each represents and warrants as follows:

9.1.1 It is a corporation duly organized, validly existing and is in good standing under the laws of the State of Delaware, is qualified to do business and is in good standing as a foreign corporation in each jurisdiction in which the conduct of its business or the ownership of its properties requires such qualification and has all requisite power and authority, corporate or otherwise, to conduct its business as now being conducted, to own, lease and operate its properties and to execute, deliver and perform this Agreement.

9.1.2 The execution, delivery and performance by it of this Agreement have been duly authorized by all necessary corporate action and do not and will not (i) require any additional consent or approval of its stockholders beyond the approvals already obtained; (ii) violate any provision of any law, rule, regulations, order, writ, judgment, injunctions, decree, determination award presently in effect having applicability to it or any provision of its certificate of incorporation or by-laws; or (iii) result in a breach of or constitute a default under any material agreement, mortgage, lease, license, permit or other instrument or obligation to which it is a Party or by which it or its properties may be bound or affected.

9.1.3 This Agreement is a legal, valid and binding obligation of it enforceable against it in accordance with its terms and conditions, except as such enforceability may be limited by applicable bankruptcy, insolvency, moratorium, reorganization or similar laws, from time to time in effect, affecting creditor's rights generally.

9.1.4 It is not under any obligation to any person, or entity, contractual or otherwise, that is conflicting or inconsistent in any respect with the terms of this Agreement or that would impede the diligent and complete fulfillment of its obligations.

9.1.5 It has good and marketable title to or valid leases or licenses for, all of its properties, rights and assets necessary for the fulfillment of its responsibilities under the Research Program, subject to no claim of any third party other than the relevant lessors or licensors.

9.2 REPRESENTATIONS AND WARRANTIES OF RIGEL.

9.2.1 LICENSES GRANTED. Rigel represents and warrants to Pfizer that it has the right to grant the licenses granted pursuant to this Agreement, and that the licenses so granted do not conflict with or violate the terms of any agreement between Rigel and any third party.

9.2.2 FINANCIAL STABILITY. Rigel represents and warrants as of the Effective Date that it has received subsequent to October 31, 1998 cash aggregating at least $7 million from equity investment and at least $3 million from license fees and research support which, together with other cash on hand and projected cash receipts, is sufficient to meet its projected cash expenses during the next following 18 months exclusive, in each case, respectively, of cash received or to be received from Pfizer and of cash Rigel is required to

expend to perform fully its obligations under the Research Program. Rigel further represents and warrants that during the Research Period it will continue to maintain sufficient financial resources to perform fully its obligations under the Research Program and will furnish to Pfizer, not earlier than January 31, 1999 or more often than annually thereafter, within sixty (60) days after receipt of Pfizer's written request therefor, reasonable evidence of sufficient financial resources to perform fully its remaining obligations under the Research Program; provided, however, the information contained in, and any information furnished pursuant to Pfizer's request under, this Section 9.2.2 is Confidential Information of Rigel and is subject to the requirements of Article 4 of this Agreement.

9.2.3 GOVERNMENTAL CONSENTS. No consent, approval, qualification, order or authorization of, or filing with, any local, state, or federal governmental authority is required on the part of Rigel in connection with Rigel's valid execution, delivery, or performance of this Agreement.

9.2.4 CAPITALIZATION AND VOTING RIGHTS. The authorized capital of Rigel consists, or will consist immediately prior to the Effective Date, of:

(a) Preferred Stock. 22,000,000 shares of Preferred Stock, par value $.001, of which 665,000 shares have been designated Series A Preferred Stock, all of which are issued and outstanding; 7,675,000 shares have been designated Series B Preferred Stock, of which 7,500,000 are issued and outstanding; 8,000,000 shares have been designated Series C Preferred Stock, of which 7,386,843 are issued and outstanding; and 5,660,000 shares of Series D Preferred Stock, of which 3,481,864 are issued and outstanding (before giving effect to any transactions with Pfizer). The rights, privileges and preferences of the Series A, Series B, Series C and Series D Preferred Stock are as stated in the restated certificate of incorporation.

(b) Common Stock. 35,000,000 shares of common stock, par value $.001 ("Common Stock"), of which 2,675,333 shares are issued and outstanding.

(c) The outstanding shares of Series A Preferred Stock, Series B Preferred Stock, Series C Preferred Stock, and Common Stock have been duly authorized and validly issued, are fully paid and nonassessable, and were issued in accordance with the registration or qualification provisions of the Securities Act and any relevant state securities laws or pursuant to valid exemptions therefrom.

(d) Except for (i) the conversion privileges of the Series A, Series B, Series C, and Series D Preferred Stock, (ii) the rights provided in paragraph 2.3 of a certain Investor Rights Agreement separately furnished to Pfizer, (iii) a warrant to purchase 175,000 shares of Series B Preferred Stock, (iv) a warrant to purchase 131,578 shares of Series C Preferred Stock, and (v) shares to be issued to Pfizer under a certain stock purchase agreement executed on even date herewith, there are not outstanding any options, warrants, rights (including conversion or preemptive rights and rights of first refusal), proxy or stockholder agreements or agreements of any kind for the purchase or acquisition from Rigel of any of its securities. In addition, Rigel has reserved 5,325,000 shares of its Common Stock for purchase upon exercise of options to be granted in the future under Rigel's 1997 Stock Option Plan (the "Option Plan"). Rigel is not a party or subject to any agreement or understanding, and, to the best of Rigel's knowledge, there is no agreement or understanding between any persons that affects or relates to the voting or giving of written consents with respect to any security or the voting by a director of Rigel.

9.2.5 SUBSIDIARIES. As of the Effective Date, Rigel does not own or control, directly or indirectly, any interest in any other corporation, partnership, limited liability company, association, or other business entity. Rigel is not a participant in any joint venture, partnership, or similar arrangement.

9.2.6 PERMITS. Rigel has all franchises, permits, licenses, and any similar authority necessary for the conduct of its business as now being conducted by it, the lack of which could materially and adversely affect the business, properties, prospects, or financial condition of Rigel, and believes it can obtain, without undue burden or expense, any similar authority for the conduct of its business as presently planned to be conducted. Rigel is not in default in any material respect under any of such franchises, permits, licenses or other similar authority.

9.2.7 COMPLIANCE WITH OTHER INSTRUMENTS. Rigel is not in violation or default in any material respect of any provision of its restated certificate of incorporation or bylaws or in any material respect of any provision of any mortgage, indenture, agreement, instrument, or contract to which it is a party or by which it is bound or, to the best of its knowledge, of any federal or

state judgment, order, writ, decree, statute, rule, regulation or restriction applicable to Rigel. The execution, delivery, and performance by Rigel of this Agreement and the consummation of the transactions contemplated hereby and thereby, will not result in any such violation or be in material conflict with or constitute, with or without the passage of time or giving of notice, either a material default under any such provision or an event that results in the creation of any material lien, charge, or encumbrance upon any assets of Rigel

or the suspension, revocation, impairment, forfeiture, or nonrenewal of any material permit, license, authorization, or approval applicable to Rigel, its business or operations, or any of its assets or properties.

9.2.8 LITIGATION. There is no action, suit, proceeding, or investigation pending or currently threatened against Rigel that questions the validity of this Agreement or the right of Rigel to enter into this Agreement, or to consummate the transactions contemplated hereby, or that might result, either individually or in the aggregate, in any material adverse change in the assets, business, properties, prospects, or financial condition of Rigel, or in any material change in the current equity ownership of Rigel. The foregoing includes, without limitation, any action, suit, proceeding, or investigation pending or currently threatened involving the prior employment of any of Rigel's employees, their use in connection with Rigel's business of any information or techniques allegedly proprietary to any of their former employers, their obligations under any agreements with prior employers, or negotiations by Rigel with potential backers of, or investors in, Rigel or its proposed business. Rigel is not a party to or, to the best of its knowledge, named in or subject to any order, writ, injunction, judgment, or decree of any court, government agency, or instrumentality. There is no action, suit, proceeding or investigation by Rigel currently pending or that Rigel currently intends to initiate.

9.2.9 DISCLOSURE. Rigel has provided Pfizer with all the information reasonably available to it without undue expense that Pfizer has requested for deciding whether to enter into this Agreement. This Agreement does not contain any untrue statement of a material fact or, to the best of Rigel's knowledge, omits to state a material fact necessary to make the statements made by Rigel herein not misleading.

9.2.10 FINANCIAL STATEMENTS. Rigel has delivered to Pfizer its unaudited balance sheet as at August 31, 1998 and unaudited statement of income and cash flows for the eight months ending August 31, 1998 (collectively, the "Financial Statements"). The Financial Statements, have been prepared in accordance with generally accepted accounting principles applied on a consistent basis throughout the periods indicated, except as disclosed therein, and present fairly the financial condition and position of Rigel as of August 31, 1998; provided, however, that the unaudited financial statements are subject to normal recurring year-end audit adjustments (which are not expected to be material), and do not contain all footnotes required under generally accepted accounting principles.

9.2.11 CHANGES. Since August 31, 1998 there has not been:

(a) any damage, destruction or loss, whether or not covered by insurance, materially and adversely affecting the business, properties, prospects, assets, liabilities or financial condition of Rigel (as such business is presently conducted and as it is presently proposed to be conducted);

(b) any waiver or compromise by Rigel of a valuable right or of a material debt owed to it;

(c) any satisfaction or discharge of any lien, claim, or encumbrance or payment of any obligation by Rigel, except in the ordinary course of business and that is not

material to the business, properties, prospects, or financial condition of Rigel (as such business is presently conducted and as it is presently proposed to be conducted);

(d) any sale, assignment, or transfer of any patents, trademarks, copyrights, trade secrets, or other intangible assets;

(e) any resignation or termination of employment of any key officer of Rigel and Rigel, to the best of its knowledge, does not know of the impending resignation or termination of employment of any such officer;

(f) any mortgage, pledge, transfer of a security interest in, or lien, created by Rigel, with respect to any of its material properties or assets, except liens for taxes not yet due or payable;

(g) any loans or guarantees made by Rigel to or for the benefit of its employees, stockholders, officers, or directors, or any members of their immediate families, other than travel advances and other advances made in the ordinary course of its business;

(h) any declaration, setting aside, or payment of any dividend or other distribution of Rigel's assets in respect of any of Rigel's capital stock, or any direct or indirect redemption, purchase, or other acquisition of any of such stock by Rigel;

(i) any material adverse change in the business, property, assets, liabilities, financial condition or results of operations of Rigel;

(j) any change (individually or in the aggregate), except in the ordinary course of business, in the contingent obligations of Rigel by way of guarantee, endorsement, indemnity, warranty or otherwise;

(k) except in the ordinary course of business, any material change in the compensation arrangement of any of Rigel's employees, officers or directors; or

(l) to the best of Rigel's knowledge, any other event or condition of any character that might materially and adversely affect the business, properties, prospects, or financial condition of Rigel (as such business is presently conducted and as it is presently proposed to be conducted).

9.2.12 PATENTS AND TRADEMARKS. To the best of its knowledge (but without having conducted any special investigation), Rigel owns or possesses sufficient legal rights to all patents, trademarks, service marks, trade names, copyrights, trade secrets, licenses, information, and proprietary rights and processes (including technology currently licensed from Stanford University) necessary for its business as now conducted and as proposed to be conducted without any conflict with, or infringement of the rights of, others. Rigel currently licenses certain technology from Stanford University (the "Licensed Technology") on an "as is" basis, with no representation or warranty from Stanford University that such technology does not infringe the proprietary rights of others. To Rigel's knowledge, Rigel has not, as of the date hereof, received any claims from any third party alleging that the use of the Licensed Technology infringes the

proprietary rights of such party. Except for agreements with its own employees or consultants and standard end-user license agreements, there are no outstanding options, licenses, or agreements of any kind relating to the foregoing, nor is Rigel bound by or a party to any options, licenses, or agreements of any kind with respect to the patents, trademarks, service marks, trade names, copyrights, trade secrets, licenses, information, and proprietary rights and processes of any other person or entity, other than the license agreements with Janssen Pharmaceutica N.V., Stanford University, SUNY, and BASF. Rigel has not received any communications alleging that Rigel has violated or, by conducting its business as proposed, would violate any of the patents, trademarks, service marks, trade names, copyrights, trade secrets, or other proprietary rights or processes of any other person or entity. Rigel is not aware that any of its employees is obligated under any contract (including licenses, covenants, or commitments of any nature) or other agreement, or subject to any judgment, decree, or order of any court or administrative agency, that would interfere with the use of such employee's best efforts to promote the interests of Rigel or that would conflict with Rigel's business as proposed to be conducted. Neither the execution nor delivery of this Agreement, nor the carrying on of Rigel's business by the employees of Rigel, nor the conduct of Rigel's business as proposed, will, to the best of Rigel's knowledge, conflict with or result in a breach of the terms, conditions, or provisions of, or constitute a default under, any contract, covenant, or instrument under which any of such employees is now obligated. Rigel is not aware of any violation by a third party of any of Rigel's patents, licenses, trademarks, service marks, tradenames, copyrights, trade secrets or other proprietary rights.

9.2.13 EMPLOYEES; EMPLOYEE COMPENSATION. There is no strike, labor dispute or union organization activities pending or, to the best of Rigel's knowledge, threatened between it and its employees. None of Rigel's employees belongs to any union or collective bargaining unit. To the best of its knowledge, Rigel has complied in all material respects with all applicable state and federal equal opportunity and other laws related to employment. To the best of Rigel's knowledge, no employee of Rigel is or will be in violation of any judgment, decree, or order, or any term of any employment contract, patent disclosure agreement, or other contract or agreement relating to the

relationship of any such employee with Rigel, or any other party because of the nature of the business conducted or presently proposed to be conducted by Rigel or to the use by the employee of his or her best efforts with respect to such business. Rigel is not a party to or bound by any currently effective employment contract, deferred compensation agreement, bonus plan, incentive plan, profit sharing plan, retirement agreement, or other employee compensation agreement, except as entered into in the ordinary course of business. Rigel is not aware that any officer or key employee, or that any group of key employees, intends to terminate their employment with Rigel, nor does Rigel have a present intention to terminate the employment of any of the foregoing. Subject to general principles related to wrongful termination of employees, the employment of each officer and employee of Rigel is terminable at the will of Rigel.

9.2.14 PROPRIETARY INFORMATION AND INVENTIONS AGREEMENTS. Each employee and officer of Rigel has executed a Proprietary Information and Inventions Agreement. Each consultant to Rigel has executed a Consulting Agreement containing confidentiality and assignment of inventions provisions similar to those included in the Proprietary Information and Inventions Agreement.

9.2.15 TAX RETURNS, PAYMENTS, AND ELECTIONS. Rigel has timely filed all tax returns and reports (federal, state and local) as required by law. These returns and reports are true and correct in all material respects. Rigel has paid all taxes and other assessments due, except those contested by it in good faith. Rigel has not elected pursuant to the Internal Revenue Code of 1986, as amended ("Code"), to be treated as an S corporation or a collapsible corporation pursuant to Section 1362(a) or Section 341(f) of the Code, nor has it made any other elections pursuant to the Code (other than elections that relate solely to methods of accounting, depreciation, or amortization) that would have a material effect on the business, properties, prospects, or financial condition of Rigel. Rigel has never had any tax deficiency proposed or assessed against it and has not executed any waiver of any statute of limitations on the assessment or collection of any tax or governmental charge. None of Rigel's federal income tax returns and none of its state income or franchise tax or sales or use tax returns has ever been audited by governmental authorities.

9.2.16 INSURANCE. Rigel has in full force and effect fire and casualty insurance policies, with extended coverage, in amounts customary for companies similarly situated to Rigel.

9.2.17 ENVIRONMENTAL AND SAFETY LAWS. Rigel is not in violation of any applicable statute, law, or regulation relating to the environment or occupational health and safety, and to the best of its knowledge, no material expenditures are or will be required in order to comply with any such existing statute, law, or regulation.

9.2.18 REAL PROPERTY HOLDING CORPORATION. Rigel is not a real property holding corporation within the meaning of Code section 897(c)(2) and any regulations promulgated thereunder.

9.2.19 FDA APPROVAL. The U.S. Food and Drug Administration has not delivered a letter of nonapproval, nor threatened to deliver such a letter, with respect to any product manufactured, marketed, licensed or developed by Rigel, or any product which Rigel intends to manufacture, market, license or develop.

9.2.20 INVESTMENT COMPANY ACT. Rigel is not an "investment company", or a company "controlled" by an "investment company", within the meaning of the Investment Company Act of 1940, as amended.

10. COVENANTS OF RIGEL AND PFIZER OTHER THAN REPORTING REQUIREMENTS.

Throughout the term of the Agreement, Rigel and Pfizer each shall:

10.1 maintain and preserve its corporate existence, rights, franchises and privileges in the jurisdiction of its incorporation, and qualify and remain qualified as a foreign corporation in good standing in each jurisdiction in which such qualification is from time to time necessary or desirable in view of their business and operations or the ownership of their properties.

10.2 comply in all material respects with the requirements of all applicable laws, rules, regulations and orders of any government authority to the extent necessary to conduct the

Research Program, except for those laws, rules, regulations, and orders it may be contesting in good faith.

11. INDEMNIFICATION.

Pfizer will indemnify Rigel for damages, settlements, costs, legal fees and other expenses incurred in connection with a claim against Rigel based on a Licensed Product or any action or omission of Pfizer, its agents or employees whether such claims allege negligence, willful misconduct or strict liability, related to the obligations of Pfizer under this Agreement. Pfizer, in its sole discretion, shall choose legal counsel, shall control the defense of such claim or action and shall have the right to settle same on such terms and conditions it deems advisable.

12. NOTICES.

All notices and invoices shall be in writing mailed via certified mail, return receipt requested, courier, or facsimile transmission with transmission confirmed addressed as follow, or to such other address as may be designated from time to time:

IF TO PFIZER: To Pfizer at its address as set forth at the beginning of this Agreement.
Attention: President, Central Research
with copy to: Office of the General Counsel
Fax:

IF TO RIGEL: Rigel at its address as set forth at the beginning of this Agreement.
Attention: President
Fax: (408) 736-1588

Notices shall be deemed given as of the date received or five (5) days after dispatch.

13. GOVERNING LAW.

This Agreement shall be governed by and construed in accordance with the laws of the State of New York.

14. MISCELLANEOUS.

14.1 BINDING EFFECT. This Agreement shall be binding upon and inure to the benefit of the Parties and their respective legal representatives, successors and permitted assigns.

14.2 HEADINGS. Paragraph headings are inserted for convenience of reference only and do not form a part of this Agreement.

14.3 COUNTERPARTS. This Agreement may be executed simultaneously in two or more counterparts, each of which shall be deemed an original. Signatures may be transmitted via facsimile, thereby constituting the valid signature and delivery of this Agreement.

14.4 AMENDMENT, WAIVER. This Agreement may be amended, modified, superseded or canceled, and any of the terms may be waived, only by a written instrument executed by each Party or, in the case of waiver, by the Party or Parties waiving compliance. The delay or failure of any Party at any time or times to require performance of any provisions shall in no manner affect the rights at a later time to enforce the same. No waiver by any Party of any condition or of the breach of any term contained in this Agreement, whether by conduct, or otherwise, in any one or more instances, shall be deemed to be, or considered as, a further or continuing waiver of any such condition or of the breach of such term or any other term of this Agreement.

14.5 NO THIRD PARTY BENEFICIARIES. No third party including any employee of any Party to this Agreement, shall have or acquire any rights by reason of this Agreement. Nothing contained in this Agreement shall be deemed to constitute the Parties partners with each other or any third party.

14.6 ASSIGNMENT AND SUCCESSORS. This Agreement may not be assigned by either Party, except that each Party may assign this Agreement and the rights and interests of such Party, in whole or in part, to any of its Affiliates, any purchaser of all or substantially all of its assets or to any successor corporation resulting from any merger or consolidation of such Party with or into such corporations.

14.7 FORCE MAJEURE. Neither Pfizer nor Rigel shall be liable for failure of or delay in performing obligations set forth in this Agreement, and neither shall be deemed in breach of its obligations, if such failure or delay is due to natural disasters or any causes reasonably beyond the control of Pfizer or Rigel.

14.8 SEVERABILITY. If any provision of this Agreement is or becomes invalid or is ruled invalid by any court of competent jurisdiction or is deemed unenforceable, it is the intention of the Parties that the remainder of the Agreement shall not be affected so long as the essential benefits of this Agreement remain enforceable and obtainable.

14.9 INTEGRATION. This Agreement supersedes all other agreements and understandings between the parties with respect to the subject matter discussed herein.

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their duly authorized representatives.

Agreed: Pfizer Inc and Affiliates	Agreed: Rigel Pharmaceuticals, Inc. and Affiliates
By: /s/ George M. Milne Jr.	By: /s/ James M. Gower
George M. Milne, Jr.	James M. Gower
President	Chief Executive Officer
Pfizer Central Research	Rigel Pharmaceuticals, Inc.
Date: 1/29/99	Date 1/26/99

EXHIBIT A

RIGEL PATENT RIGHTS

<TABLE>
<CAPTION>

LICENSED TECHNOLOGIES	TITLE/MATERIAL	INVENTOR	PATENT FILING DATE	
<S>	<C>	<C>	<C>	<C>
1.	Phoenix and 293T cells lines	Garry Nolan, Stanford University	-	Non-Exclusive license 10/7/96
2.	Phoenix and 293T cells lines	Garry Nolan, Stanford University	-	Exclusive license 8/18/97
3A. USSN 08,589,109	Methods for Screening for Transdominant Effector Peptides and RNA Molecules	Garry Nolan & Michael Rothenberg, assigned to Stanford University	1/23/96	Technology licensed by Rigel 10/7/96
3B. USSN 08,787,738	Methods for Screening for Transdominant Effector Peptides and RNA Molecules	Garry Nolan & Michael Rothenberg, assigned to Stanford University	1/23/97	CIP
3C. PCT US97/01048	Methods for Screening for Transdominant Effector Peptides and RNA Molecules	Garry Nolan & Michael Rothenberg, assigned to Stanford University	1/23/97	PCT
4. US patents # 5,283,173 5,468,614 5,667,973	A Genetic System to Detect Protein-Protein Interactions	Stanley Fields & Ok-Kyu Song, assigned to the Research Foundation of SUNY (Stonybrook)	1/24/90; continued 2/1/94; continued 9/16/97	Technology licensed 1/12/98

5. Provisional application # 60,042,576, and 60,054,623; (replaced by application 09,053,614)	Detection of Molecular Interactions by Reporter Subunit Complementation	Helen Blau, assigned to Stanford University	4/2/97 8/4/97 4/1/98	Technology licensed by Rigel 3/27/98
6. (TET system includes 16 patents)	Tetracycline Regulated Expression Technology: The TET System	BASF Bioresearch Corp.		Technology licensed 5/1/98

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PATENTS	TITLE	AUTHOR	PATENT FILING DATE	
<S>	<C>	<C>	<C>	<C>
1A. USSN 08,589,911	Methods for Screening for Transdominant Intracellular Effector Peptides and RNA Molecules	Garry Nolan	1/23/96	Assigned to Rigel 10/20/97
1B. USSN 08,789,333	Methods for Screening for Transdominant Intracellular Effector Peptides and RNA Molecules	Garry Nolan	1/23/97	CIP
1C. USSN 08,963,368	Methods for Screening for Transdominant Intracellular Effector Peptides and RNA Molecules	Garry Nolan	11/3/97	divisional
1D. PCT US97/01019	Methods for Screening for Transdominant Intracellular Effector Peptides and RNA Molecules	Garry Nolan	1/23/97	PCT
2. USSN 08,873,601	Combinatorial Enzymatic Complexes	Garry Nolan & Donald Payan	6/12/97	Assigned to Rigel 9/9/97
3. USSN 09,047,119	Small Molecule Library Screening Using FACS	Donald Payan	3/24/98	
4. 09,050,863	Mammalian Protein Interaction Cloning System	Ying Luo, Betty Huang, & Donald Payan	3/30/98	
5. 60,080,444	Peptides Causing Formation of Compact Structures	Dave Anderson	4/2/98	
6. 09,076,624	Methods and Compositions for Screening for Modulators of IgE Synthesis, Secretion and Switch Rearrangement	Dave Ferrick, Susan Swift, Randy Armstrong, Bryan Fox	5/12/98	
7A. 09,133,944	Shuttle Vectors	Ying Luo, Peiwen Yu, Jim Lorens	8/14/98	
7B.	Shuttle Vectors	Ying Luo, Peiwen Yu, Jim Lorens	In process	CIP
8.	Green Fluorescent Protein Fusions with Random Peptides	David Anderson	10/9/98	

</TABLE>

EXHIBIT B

RESEARCH PLAN

1. GOALS

The goal of this collaboration between Rigel and Pfizer is to identify novel and selective elements of the IL-4 signaling pathway that are suitable targets for an IgE synthesis inhibitor, lead identification program.

2. RESEARCH PLAN

The research strategy for the first two years of the Pfizer-Rigel collaboration is shown in FIGURE 1. During this time, research activities will take place primarily at Rigel towards the goal of discovering novel Molecular Targets in the IL-4 signaling pathway that can be further developed by Pfizer into high throughput screens (HTS) at Pfizer to find agents to inhibit IL-4 signaling and IgE synthesis for the treatment of allergic disease and asthma. In brief, Rigel uses intracellular retrovirus expression of peptide libraries in an IL-4 responsive reporter cell line to discover peptide inhibitors of the IL-4 signaling pathway. The peptide inhibitors are validated by showing their selectivity in inhibiting IL-4 directed IgE synthesis over IL-10 directed IgG synthesis. The peptide inhibitors are used to isolate their protein ligands using Yeast Two Hybrid (YTH) technology, and then these ligands will be valided for their effect on IgE synthesis at Rigel using a combination of IN VITRO mutagenesis and further YTH pathway mapping.

2.1 DELIVERABLES AND TIMELINE

2.1.1 RESEARCH ACTIVITIES, 0-12 MONTHS:

DELIVERABLE 1 (D1)--ISOLATION AND CONFIRMATION OF INHIBITORY PEPTIDES:

(a) (8 MONTHS) Rigel will endeavor to isolate specific peptide inhibitors of IL-4-induced, B cell germline epsilon transcription, from stem loop peptide libraries (2x10(9) component complexity) using a Fas-mediated apoptosis cell survival assay. The greater the number of peptides actually expressed in the reporter cell line, the greater the chances of finding novel Molecular Targets, so every reasonable effort will be made to maximize the representation of the peptide library in the reporter cell line. However, taking transfection efficiency into account, no less than 10(8) components will be have been expressed in the B-cell reporter cell line. The iterative enrichment of inhibitory peptides and their characterization will be carried out by Rigel as shown in Figure 2.

(b) (12 MONTHS) As noted in Figure 2, Rigel will endeavor to confirm that individual peptide inhibitors confer the IL-4 resistant phenotype in a Fas-mediated apoptosis cell survival assay. The capacity of this assay would allow 100+ peptide inhibitors to be taken forward through this assay for confirmation.

2.1.2 RESEARCH ACTIVITIES, 12-18 MONTHS:

DELIVERABLE 2 (D2)--IgE SYNTHESIS INHIBITION AND SPECIFICITY OF INDIVIDUAL PEPTIDE HITS:

Rigel will endeavor to demonstrate that recovered single peptide hits inhibit IgE synthesis SELECTIVELY over IgG synthesis as follows:

(a) Measure IgE versus IgG secretion/switching inhibition in a cytokine stimulated BL16 B-cell line. The goal is that the inhibitory peptide will inhibit IgE levels in the media produced by the IgM+ BL16 cell line stimulated with IL-4 by 20 fold over an irrelevant peptide control. If the peptide also inhibits IL-10 driven IgG levels from the IgM+ BL16 cell line, the goal will be that the peptide will inhibit IgE levels by 20 fold more than IgG. Secreted antibody levels will be measured in the media by ELISA. Because of the higher throughput of the BL16 assay (capacity = 100+ peptides) versus the primary PBL assay (capacity = 10 peptides), it is expected that the BL16 assay will be used to rapidly select peptides that will serve as baits in YTH screening, while the PBL assay will only be performed on those peptides whose ligands are not known components of the IL-4 signaling pathway.

(b) Confirm that the peptide inhibitor meets the same criteria as in D2a in primary cells by performing similar experiments to those in D2a in cytokine stimulated IgM+ enriched human peripheral blood lymphocytes or IgM+ enriched human tonsillar B-cells. Because of the low throughput and variability of this assay, those peptides that are the binding partners of known members of the IL-4 signaling pathway will not be tested in this assay.

D2 CRITERIA: Section 2.1.2(a) shall be known as D2a criteria, and Section 2.1.2(b) above shall be known as D2b criteria.

DELIVERABLE 3 (D3)--CLONING OF FULL LENGTH CDNAS OF PROTEINS BINDING OF INHIBITORY PEPTIDES:

Rigel will deliver full length sequences of protein binding partners of inhibitory peptides. Up to 20 functionally active single peptide hits will be used as bait in a YTH system (YTH level 1) to identify cDNAs encoding the target protein partners of the active peptides. Rigel will perform bioinformatic analysis to identify the isolated clones. Pfizer will also contribute bioinformatic analysis in order to attempt to identify some of these clones based on homology to sequences in public databases and private databases available to Pfizer. Bioinformatics, RACE (Rapid Amplification of CDNA Ends), or cDNA cloning will be used by Rigel to obtain full length cDNA sequences encoding up to 12 independent target proteins from the cDNA sequences isolated using YTH.

D3 MILESTONE CRITERIA: D3 criteria comprise meeting each of the following: (1) The cDNA is the ligand of an inhibitory peptide that met the criteria in D2a and D2b. (2) The cDNA contains the full length coding region, and is either the only ligand for a given peptide inhibitor or can be conclusively shown to be the ligand responsible for the IL-4 inhibition. (3) At the time of its discovery, the cDNA did not encode a protein already known in the literature or to Pfizer to be a component of the IL-4 signaling pathway whose inhibition would be expected to have a specific effect on the germline epsilon promoter. These proteins must include the following: IL-4R alpha chain, IL-4R gamma chain, Jak kinases, STAT6, as well as two other proteins (a transcription factor and an enzyme) whose role is unpublished and identity is known to Pfizer through confidential sources. The identity of these proteins are as follows: The transcription factor Bc16, and the Pim family of Ser/Thr Kinases, particularly Pim-2.
[to be added at the time of the execution of the Agreement.] (4) The cDNA is not identical or overlapping with another cDNA for which a D3 milestone has already been triggered.

At Pfizer's sole, unfettered discretion, a D3 milestone may be paid to Rigel by Pfizer in the absence of one or more of the first three criteria being met.

2.1.3 RESEARCH ACTIVITIES, 18-24 MONTHS

DELIVERABLE 4 (D4)--VALIDATION OF CDNAS IDENTIFIED IN DELIVERABLE 3 (D3):

(a) Rigel will endeavor to complete mutagenesis target validation data for two proteins identified in Deliverable 3. Greater than one hundred mutants will be generated for each target by error prone PCR and delivered via retrovirus constructs to the Fas-mediated apoptosis survival assay to select for dominant negative mutants that confer the IL-4 resistant phenotype. If dominant negatives are found, selective inhibition of IgE synthesis over IgG synthesis will be measured as in Deliverable 2a and 2b above, with the same throughput for the BL16 and PBL assays.

(b) Rigel will endeavor to deliver additional protein targets and pathway mapping in the IL-4/germline epsilon pathway. Up to five full length cloned protein targets identified in Deliverable 3 will be used as bait in YTH experiments (YTH level 2) to identify further protein binding partners which interact with each clone in order to map the IL-4 signaling pathway and validate the role of these proteins in IL-4 signaling. If the protein binding partner of an inhibitory peptide were to be found to bind to a known member of the IL-4 signaling pathway, this would represent partial validation of this D3 protein in the IL-4 signaling pathway. Full length clones for up to 8 of the binding partners will be sought in preparation for possible future YTH level 3 screening during an optional 3rd year of the Pfizer-Rigel collaboration.

D4 MILESTONE CRITERIA: D4 criteria comprise meeting either one of the following two criteria for a D3 cDNA clone or its encoded protein. (a) Successful selection of one or more dominant negative mutants of a cDNA whose effect after intracellular retroviral expression satisfies the criteria applied to inhibitory peptides in D2a and D2b. (b) Demonstration in YTH level 2 that the protein encoded by a given cDNA binds to a known member of the IL-4 signal transduction pathway. Specific qualifying components would be all those noted in the D3 Milestone Criteria.

At Pfizer's sole, unfettered discretion, a D4 milestone may be paid to Rigel by Pfizer in the absence of one or more of the criteria being met.

2.2 PROGRAM TECHNOLOGIES

Certain reagents will be enabling to Pfizer's efforts to validate Molecular Targets, to progress Molecular Targets to the HTS phase, and to engage in research in the IgE synthesis inhibition area. Since they are not explicitly stated elsewhere, the following reagents will be considered Program Technologies: the IL-4 driven Fas reporter cell line, an IL-4 driven GFP reporter cell line, the BL16 cell line derivative used in this collaboration, any useful derivatives of these that may be used in the course of the collaboration, other enabling cell lines specifically made for this collaboration, and the PBL assay.

2.3 PROGRESSION OF MOLECULAR TARGETS AT PFIZER

Once potential Molecular Targets are available, Pfizer will have the sole unfettered discretion of which to select for progression to HTS and beyond. Pfizer will perform target validation experiments and will adapt the Molecular Target for HTS. From this point, a Pfizer project team will follow a standard drug discovery progression from lead discovery, candidate optimization, and candidate validation using IN VITRO and IN VIVO models. Compounds satisfying candidate criteria will follow the usual Pfizer preclinical development program (i.e. General Pharmacology, Genetic Toxicology, and Exploratory Toxicology studies) to the recommendation for development (RFD) stage.

After a Candidate Alert Notice ("CAN") is issued, General Pharmacology and Exploratory Toxicology studies in two species will be conducted. A RFD (or CANTOX) document will issue by approval of Pfizer's Early Development Management Team after a satisfactory completion of General Pharmacology and the 14-day rat and dog (or monkey) Exploratory Toxicology, including histopathology, evaluations. For studies in man, Pfizer policy is that a clinical candidate should have a safety margin of 10x between a predicted human efficacious dose (plasma concentration and/or exposure taken into account) and a non-observable-adverse-effect-level (NOAEL).

Rigel-Pfizer Collaboration

FIGURE 1

FIGURE 2

RIGEL: SELECTION OF PEPTIDE INHIBITORS OF IL-4 SIGNALING (0-12 months)

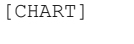

EXHIBIT 10.8

COLLABORATION AGREEMENT

THIS COLLABORATION AGREEMENT ("Agreement") is entered into as of May 26th, 1999 ("Effective Date") by and between RIGEL PHARMACEUTICALS, INC., a Delaware corporation ("Rigel") with its offices at 240 East Grand Avenue, South San Francisco, CA 94080, and NOVARTIS PHARMA AG, a Swiss corporation ("Novartis") with offices at Lichtstrasse 35, CH-4058, Basel, Switzerland (collectively, "Parties"; individually, a "Party").

RECITALS

WHEREAS, Rigel is a leader in the discovery and validation of intracellular target molecules involved in the modulation of human disease; and

WHEREAS, Novartis is engaged in the research, development, marketing, manufacture and distribution of pharmaceutical compounds useful in treating or preventing human diseases and conditions; and

WHEREAS, Rigel and Novartis desire to enter into a collaborative relationship to conduct research on intracellular target molecules and to discover, develop and manufacture pharmaceutical products useful for treating or preventing diseases associated with human disease; and

WHEREAS, Novartis is purchasing two million (2,000,000) shares of Rigel Series D Preferred Stock with a total value of US$4 million pursuant to a stock purchase agreement between the Parties of even date herewith (the "Stock Purchase Agreement"), and the Parties are further entering into an Equity Option Agreement pursuant to which Novartis may purchase up to an additional US$10 million in value of Rigel equity;

NOW, THEREFORE, in consideration of the foregoing and the covenants and promises contained in this Agreement, the Parties agree as follows:

1. DEFINITIONS

As used herein, the following terms (whether used in their singular or plural form) shall have the following meanings:

"AFFILIATE" shall mean, with respect to a Party to this Agreement, any other entity, whether de jure or de facto, which directly or indirectly controls, is controlled by, or is under common control with, such Party. A business entity or Party shall be regarded as in control of another business entity if it owns, or directly or indirectly controls, at least fifty percent (50%) (or such lesser percentage which is the maximum allowed to be owned by a foreign entity in a particular jurisdiction) of the voting stock or other ownership interest of the other entity, or if it directly or indirectly possesses the power to direct or cause the direction of the management and policies of the other entity by any lawful means whatsoever.

"AT-NOVARTIS PROJECT" shall mean a Program of Research performed by Novartis as provided in Section 4.2 hereof.

"B-CELL PROJECT" shall mean the Program of Research directed to the identification of Novel Validated Targets involved in the process of B-Cell activation, as the Program of Research is more fully described in Exhibit A-2 hereto.

"COLLABORATION PROJECT" shall mean a Joint Project or an At-Novartis Project.

"COMMENCEMENT DATE" shall mean the date upon which a Collaboration Project shall commence as set forth in Exhibit B or as determined pursuant to the provisions of Section 2.2 hereof.

"COMPOUND SCREENING" shall mean the use of a primary assay for testing biological or chemical materials, including chemical materials coming out of high-throughput screening, to determine whether they show pharmaceutically relevant activity.

"CONFIDENTIAL INFORMATION" shall mean any invention, discovery, patent application or claim, trade secret, idea, improvement or other work of authorship, any process, formula, data, program, drawing, information, price, technique, sample, compound, extract, media, vector and/or cell line and procedures and formulations for producing any such sample, compound, extract, media, vector and/or cell line, any process, formula or data relating to any research project, work in process, future development, engineering, manufacturing, marketing, servicing, financing or personnel matter relating to a Party, its present or future products, sales, suppliers, clients, customers,

employees, investors, or business, whether in oral, written, graphic or electronic form.

"CONTROL" shall mean the possession of the ability to grant a license or sublicense to know-how or patents without violating the terms of any agreement or other arrangement with, or the rights of, any Third Party.

"COOPERATION MANAGEMENT COMMITTEE" or "CMC" shall mean the committee formed pursuant to Section 3.1.

"EXCLUSIVITY TERM" shall have the meaning assigned to it in Section 5.2.

"EXTENSION FEE" shall have the meaning assigned to it in Section 7.5.

"FSC-STATUS" or "Final Selected Compound Status" shall mean the point at which a Product is declared, following Novartis' standard compound development procedures, an 'FSC Compound' or equivalent status by Novartis' Research Management Board or some other similar body, which declaration authorizes the initiation of preclinical development programs aimed, INTER ALIA, at the detailed investigation of those toxicological, bioavailability, pharmacokinetic and formulation parameters whose successful completion will allow progression of the Product to Phase I Clinical Trials.

"FTE" shall mean the equivalent of a full-time twelve (12) months (including normal vacations, sick days and holidays) work of a person, carried out by one or more employees or consultants of a Party, each of whom devotes all or a portion of his or her time to a Collaboration Project; provided, however, that each Party understands and agrees that the other Party retains complete discretion to change the identity, the frequency and time which

any individual employee devotes to a Collaboration Project. Scientific work on or directly related to a Collaboration Project to be performed by a Party's employees or consultants can include, but is not limited to, experimental laboratory work, recording and writing up results, reviewing literature and references, holding scientific discussions, managing and leading scientific staff, and carrying out Research Cooperation management duties (including service on the Cooperation Management Committee).

"JOINT INVENTION" shall have the meaning assigned to it in Section 8.1.

"JOINT PROJECT" shall mean a Program of Research which Novartis and Rigel agree will be conducted collaboratively as provided in Section 4.1 hereof.

"JOINT TECHNOLOGY" shall mean Know-How and Patents conceived or reduced to practice by at least one employee of Novartis and at least one employee of Rigel during the course of a Program of Research.

"KNOW-HOW" shall mean any and all tangible or intangible know-how, trade secret, invention (whether or not patentable), data, pre-clinical and clinical result, physical, chemical or biological material, and other information.

"LEAD COMPOUND" shall mean an active compound identified by Rigel in the course of Compound Screening on the basis of a Novel Validated Target pursuant to Section 5.6.

"MILESTONE EVENT" shall have the meaning assigned to it in Section 7.2.

"MILESTONE PAYMENT" shall have the meaning assigned to it in Section 7.2.

"NOTICE DATE" shall have the meaning assigned to it in Section 4.1.4 and 4.2.4.

"NOVARTIS KNOW-HOW" shall mean any Know-How that is necessary and useful in a Program of Research and that Novartis owns or Controls on the Effective Date, and any replication or any part of such information or material.

"NOVARTIS PATENTS" shall mean all Patents which claim inventions or discoveries necessary and useful in a Program of Research and that that Novartis owns or Controls on the Effective Date.

"NOVARTIS TECHNOLOGY" shall mean Novartis Know-How and Novartis Patents, subject to any limitation contained in the agreements under which Novartis' rights to the use of such Novartis Technology are derived.

"NOVEL VALIDATED TARGET" shall mean a specific molecule in an intracellular signaling pathway which, when bound by a specific peptide, changes in a predetermined way the phenotype of a target cell with a degree of specificity and in a manner meeting the predetermined validation criteria set by

the CMC for Joint Projects and by Novartis for At-Novartis Projects.

"PATENTS" shall mean all foreign and domestic patents (including, without limitation, extensions, reexaminations, reissues, renewals and inventors certificates) and patents issuing from patent applications (including substitutions, provisionals, divisionals, continuations and continuations-in-part).

"PHASE I CLINICAL TRIALS" shall mean first clinical trial where the Product is applied in healthy human volunteers to test safety of such Product.

"PRODUCT" shall mean a molecule in the various stages of development from identification in Compound Screening to and including commercialization, which is useful to diagnose, treat or prevent human diseases or conditions and whose principal mechanism of action by which it exerts its pharmacological activity is based upon, derived from or discovered with the use of, a Novel Validated Target.

"PROGRAM OF RESEARCH" shall mean research utilizing Rigel Technology to identify specific target molecules and peptides which bind thereto that alter a selected phenotype of a target cell population, including the use of retroviral vector and expression systems which express libraries of molecules in target cells, high-speed fluorescent cell sorting systems to identify the cells in which the selected phenotype change has occurred and two-hybrid screening assays to elaborate the intracellular interactions of the specific target molecules and other means and methods, whether or not utilizing Rigel Technology, appropriate in a particular program.

"PROGRAM PROPOSAL" shall mean a written description of a Program of Research specifying in reasonable detail the specific goals of the project including clinical objectives, target cells to be utilized, desired biologic endpoints of assays of the target cells, project time frames and resource requirements.

"PROJECT CONTACT PERSON" shall have the meaning assigned to it in Section 3.8.

"PROJECT KNOW-HOW" shall mean Know-How developed, conceived or reduced to practice by a Party in the course of a Collaboration Project.

"PROJECT PATENT" shall mean a Patent claiming Project Know-How.

"PROJECT TECHNOLOGY" shall mean Project Know-How and Project Patents.

"RESEARCH COOPERATION" shall mean the Joint Projects and the At-Novartis Projects.

"RESEARCH PERIOD" shall mean, for each Joint Project and each At-Novartis Project, five (5) years commencing as of the corresponding Commencement Date, subject to earlier termination as permitted hereby.

"RIGEL CORE TECHNOLOGY" shall mean Rigel's proprietary packaging cell lines (e.g., without limitation, that designated as Phoenix), high-speed functional genomic screening technology, two-hybrid screening assays, retroviral vector systems and expression systems that utilize these vectors to express libraries of molecules in target cells and high speed fluorescent cell sorting systems and any improvements thereon, and any Patents and Know-How relating thereto owned or Controlled by Rigel, subject to any limitation contained in the agreements under which Rigel's rights to the use of such Rigel Core Technology are derived.

"RIGEL KNOW-HOW" shall mean any Know-How other than Rigel Core Technology that is useful in a Collaboration Project and that Rigel owns or Controls on the Effective Date and any replication or any part of such information or material.

"RIGEL PATENTS" shall mean all Patents other than Rigel Core Technology which claim inventions or discoveries useful in a Collaboration Project and that are owned or Controlled by Rigel on the Effective Date.

"RIGEL TECHNOLOGY" shall mean the Rigel Patents and Rigel Know-How, subject to any limitation contained in the agreements under which Rigel's rights to the use of such Rigel Technology are derived.

"SOLE INVENTIONS" shall have the meaning assigned to it in Section 8.1.

"T-CELL PROJECT" shall mean the Program of Research directed to the identification of Novel Validated Targets involved in the process of T-Cell

activation, as the Program of Research is more fully described in Exhibit A-1 hereto.

"TERM OF AGREEMENT" shall have the meaning assigned to it in Section 11.1.

"TERRITORY" shall mean the entire world.

"THIRD PARTY" shall mean any person or entity other than Novartis, Rigel and Affiliates of either.

2. SELECTION OF PROJECTS

2.1 NOVARTIS ACCESS TO FIVE PROJECTS. Novartis may have access to up to five (5) Programs of Research of which at least two (2) will be Joint Projects and no more than three (3) will be At-Novartis Projects.

2.2 PROPOSAL FOR A PROGRAM OF RESEARCH.

2.2.1 JOINT PROJECTS. A Program of Research for a Joint Project may be proposed by Novartis or Rigel submitting to the other a Program Proposal. Within thirty (30) days of receipt of a Program Proposal the receiving party shall determine whether it has any agreement with a Third Party which would prevent it from agreeing to conduct pursuant to this Agreement the Program of Research identified in the Program Proposal and notify the proposing party accordingly. If the receiving party is free to conduct the Program of Research pursuant to this Agreement, the Parties shall meet to determine whether they will agree to conduct such Program of Research pursuant to this Agreement. If so, the CMC shall meet promptly to prepare a mutually agreeable description of the Program of Research to be attached as an exhibit to this Agreement, to specify the number of FTEs which will be utilized, the Commencement Date and the number of FTEs as well as the resources to be allocated at Novartis. If the receiving party is not free to conduct the Program of Research pursuant to this Agreement, neither Party shall have any obligation or liability to the other with respect to such Program of Research.

2.2.2 AT-NOVARTIS PROJECTS.

(a) Novartis may propose a Program of Research for an At-Novartis Project by submitting to Rigel a corresponding Program Proposal.

(b) Novartis shall have the right to proceed with such Program of Research, unless Rigel notifies Novartis in writing within thirty (30) days of receipt of a

Program Proposal (i) that in Rigel's opinion, the Program of Research as proposed by Novartis is scientifically not feasible, or (ii) that Rigel is engaged in advanced negotiations with a Third Party regarding a collaboration on a Program of Research which would conflict with the Program of Research proposed by Novartis under this Agreement, or (iii) that Rigel has initiated an internal Program of Research, as evidenced by written records, which would conflict with the Program of Research proposed by Novartis.

(c) If Rigel provides to Novartis a notice pursuant to subsection (b)(i) above, the Parties shall meet to discuss and revise the proposed Program Proposal as appropriate to address Rigel's comments and suggestions, whereafter Novartis shall have the right to proceed with such Program of Research based on the revised Program Proposal. If Rigel provides to Novartis a notice pursuant to subsection (b)(ii) or (b)(iii) above, such Program of Research may not be pursued by Novartis, and neither Party shall have any obligation or liability to the other with respect to such Program of Research.

(d) If Novartis has the right to proceed with a Program of Research as provided in this Section 2.2.2, Novartis will provide to Rigel a mutually agreeable description of the Program of Research, including the validation criteria to be applied for determining whether a molecule is a Novel Validated Target, to be attached as an exhibit to this Agreement which description shall specify the Commencement Date of the At-Novartis Project. Thereafter, the Parties will meet promptly to specify the Rigel Technology and Rigel Core Technology to be transferred and the time of the transfer thereof to Novartis pursuant to Section 4.2.5 hereof.

2.3 NUMBER AND KIND OF ADDITIONAL PROGRAMS OF RESEARCH. The parties hereby agree that the Commencement Date of the T-Cell Project shall be the Effective Date of this Agreement. Subject to Section 2.2, Novartis and Rigel will add to this Agreement two (2) additional Programs of Research prior to the first (1st) anniversary of the Effective Date and two(2) Programs of Research prior to the second (2nd) anniversary of the Effective Date.

2.4 T-CELL PROJECT. Novartis and Rigel hereby agree that the T-Cell Project is to be conducted as a Joint Project as provided in Section 4.1 and is

one of the Programs of Research referred to in Section 2.1. A mutually agreeable description of the Program of Research is set forth in Exhibit A-1. The number of FTEs and the Commencement Date for the T-Cell Project are set forth in Exhibit B-1.

2.5 B-CELL PROJECT. Novartis hereby acknowledges that Rigel has proposed the B-Cell Project as the second Joint Project in compliance with Section 2.2, and that Novartis has no agreement with a Third Party which would prevent it from agreeing to engage in the B-Cell Project pursuant to this Agreement. A mutually agreeable description of the Program of Research for the B-Cell Project is set forth in Exhibit A-2. The number of FTEs and the Commencement Date for the B-Cell Project are set forth in Exhibit B-2. Novartis will notify Rigel within ninety (90) days after the Effective Date whether it agrees that the B-Cell Project shall be conducted as the second Joint Project. If Novartis does not so agree, Rigel's proposal of the B-Cell Project shall be considered withdrawn as of the ninety-first (91st) day after the Effective Date and neither Novartis nor Rigel shall thereafter have any obligation or liability to the other with respect to the B-Cell Project.

3. RESEARCH COOPERATION GOVERNANCE

3.1 JOINT COOPERATION COMMITTEE FORMATION. The Research Cooperation established by this Agreement shall be overseen or monitored, pursuant to the provisions of Section 3.7 hereof, by a Cooperation Management Committee composed of an equal number of representatives from each Party (the "Cooperation Management Committee"). Each Party shall initially designate three (3) representatives on the CMC within ten (10) business days after the Effective Date. The addition of further representatives to the CMC, if any, shall occur pursuant to the provisions of Section 3.3.6 hereof. Each Party may, upon notice to the other Party, change its representatives to the CMC to allow for the participation of different research groups within Novartis or Rigel, as the case may be. The Parties shall agree upon the appropriate qualifications for members of the CMC. An alternate member designated by a Party may serve temporarily in the absence of a permanent member of the CMC for such Party. Each Party shall designate one of its representatives as a Co-Chair of the CMC. Each Co-Chair of the CMC will be responsible for the agenda and the minutes of alternating CMC meetings.

3.2 CMC ACTIONS. Actions by the CMC pursuant to this Agreement shall be taken only with unanimous approval of all of the representatives of the CMC. If the CMC fails to reach unanimity on a matter before it for decision, the matter shall be referred for resolution to the designated executives of the Parties identified in Section 13.2.

3.3 MEETINGS OF THE CMC. The CMC:

3.3.1 shall hold meetings at such times and places as shall be determined by the CMC (it being expected that meetings will alternate between one of Novartis' research sites on the one hand and Rigel's head offices on the other hand) but in no event shall such meetings be held in person less frequently than once every three (3) months during the entire period during which the Research Period of at least one Collaboration Project is not yet expired or terminated;

3.3.2 may conduct meetings in person or by telephone or video conference;

3.3.3 by mutual consent of the representatives of each Party, may invite other personnel of either Party to attend meetings of the CMC;

3.3.4 may act without a meeting if prior to such action a written consent thereto is signed by all members of the CMC;

3.3.5 may form and subsequently disband subcommittees with appropriate representation from each Party;

3.3.6 may increase or decrease the equal number of CMC representatives each Party can designate; and

3.3.7 may amend or expand upon the foregoing procedures for its internal operation by unanimous written consent.

3.4 MINUTES. Subject to the provisions of Section 3.1 hereof, one of the Co-chairs of the CMC will prepare, within ten (10) business days after each meeting (whether held in person or by telephone or video conference), the minutes reporting in reasonable detail the actions taken by the CMC, the status of each Collaboration Project, the then current list of Novel Validated Targets, issues requiring resolution and resolutions of previously reported

issues, which minutes are to be approved by the signature of the CMC Co-Chair of the other Party.

3.5 SUBCOMMITTEES. Any subcommittee established by the CMC shall have appropriate representation of each Party and may include representatives of a Party who are not members of the CMC. Any such subcommittee shall be subject to the CMC and shall report its activities and actions to the CMC. At the request of either Party at any time, any such committee shall be dissolved and its powers and functions returned to the CMC.

3.6 REPORTS. Novartis and Rigel shall each provide written reports at or before each CMC meeting describing its activities and results under the Research Cooperation. Such reports shall be in such form and contain such detail as the CMC shall determine.

3.7 CMC FUNCTIONS AND POWERS. The activities of the Parties under this Agreement shall be managed by the CMC only to the extent set forth herein (unless otherwise mutually agreed by the Parties). The CMC shall:

3.7.1 foster the collaborative relationship between the Parties;

3.7.2 facilitate and monitor the technology transfer under the Collaboration Projects;

3.7.3 approve the validation criteria for a Novel Validated Target within sixty (60) days of each Commencement Date;

3.7.4 pursuant to Section 5.4 and provided Novartis has requested Rigel screening thereunder, approve in advance the criteria for a Lead Compound identified by Rigel and to be reported to Novartis;

3.7.5 monitor the progress of the research in the Joint Projects;

3.7.6 monitor the status of At-Novartis Projects to allow assessment of whether or when a Milestone Payment is due;

3.7.7 review and allocate annual FTEs in the Joint Projects, within the framework of the contractually agreed funding level;

3.7.8 clear scientific publications relating to the Joint Projects, and, insofar as containing work from both Parties, relating to At-Novartis Projects, subject to the review and approval of both Parties pursuant to Section 10.3;

3.7.9 perform such other functions as elsewhere explicitly provided in this Agreement and as appropriate to further the purposes of this Agreement as mutually determined by the Parties.

3.8 PROJECT CONTACT PERSONS. Subject to the CMC, the day-to-day communication between the Parties and project coordination of each Joint Project will be performed by two (2) "Project Contact Persons", one to be appointed by each Party.

3.9 OBLIGATIONS OF PARTIES. Each one of the Parties shall have the right to inspect the other Party's records through a qualified independent Third Party, reasonably acceptable to the other Party, to determine whether the other Party's performance complies with the

terms of this Agreement, but not more frequently than once in any year during the Research Period and subject to (1) the confidentiality obligations of Article 10 and (2) any BONA FIDE obligations of confidentiality to a Third Party.

3.10 LIMITATIONS OF POWERS OF THE CMC. The CMC shall have no power to amend this Agreement and shall have only such powers as are specifically delegated to it hereunder.

4. CONDUCT OF JOINT AND AT-NOVARTIS

4.1 CONDUCT OF JOINT PROJECTS.

4.1.1 SCOPE OF JOINT PROJECTS. Each Joint Project will be conducted as a collaborative research program during its Research Period to identify and validate Novel Validated Targets. The Parties intend that these Novel Validated Targets will be suitable to enable Compound Screening to identify molecules useful for the development and manufacture of Products.

4.1.2 REVISIONS OF JOINT PROJECTS. By mutual agreement in writing the Parties may revise the scope of a Joint Project.

4.1.3 PERFORMANCE OF RESEARCH ACTIVITIES. Each Party will perform the activities assigned to it in the Program of Research for each Joint Project, or as directed by the CMC, in good scientific manner, and in compliance with all applicable good laboratory practices and applicable legal requirements to attempt to achieve efficiently and expeditiously its objectives described in the Program of Research attached to this Agreement pursuant to Section 2.2.1.

4.1.4 IDENTIFICATION OF NOVEL VALIDATED TARGETS. Rigel shall notify the CMC in writing of each Novel Validated Target identified by Rigel during the Research Period of each Joint Project promptly after its identification. Such notice shall be accompanied with a report and sufficient data which establish that the validation criteria predetermined by the CMC pursuant to Section 3.7.3 have been met. The CMC shall issue a list of the Novel Validated Targets identified in the course of such Joint Project as a part of the minutes of each CMC meeting and a final list within thirty (30) days after the end of such Research Period. The date on which Rigel has delivered the notice described in this Section 4.1.4, provided Novartis has not within ten (10) business days of receipt of said notice informed Rigel that in Novartis' opinion, the CMC-predetermined validation cirteria have not been met, shall be considered the "Notice Date" of such Novel Validated Target. If Novartis informs Rigel that in Novartis' opinion, the CMC-predetermined validation criteria have not yet been met, the matter will be discussed and brought to a decision at the next meeting of the CMC.

4.1.5 TECHNOLOGY TRANSFER. Rigel, as from time to time it may be directed by the CMC, shall transfer to Novartis at no additional cost to Novartis such Rigel Technology and Rigel Core Technology as shall be necessary for the purpose of enabling Novartis to perform its responsibilities under the applicable Program of Research of Joint Projects to identify Novel Validated Targets. Novartis may use such Rigel Technology and Rigel Core Technology pursuant to the licenses granted under this Agreement.

4.1.6 SECONDMENT. In order to further a close working relationship, the Parties may agree to provide offices and support at its facilities for the personnel of the other Party.

4.2 CONDUCT OF AT-NOVARTIS PROJECTS.

4.2.1 SCOPE OF AT-NOVARTIS PROJECTS. Each At-Novartis Project shall be performed by Novartis fully in-house to identify and validate Novel Validated Targets. It is intended that these Novel Validated Targets will be suitable to enable Compound Screening to identify molecules useful for the development and manufacture of Products.

4.2.2 REVISIONS OF AT-NOVARTIS PROJECTS. By mutual agreement in writing the Parties may revise the scope of an At-Novartis Project.

4.2.3 PERFORMANCE OF RESEARCH ACTIVITIES. Novartis will perform research in accordance with the Program of Research for each At-Novartis Project in good scientific manner, and in compliance with all applicable good laboratory practices and applicable legal requirements to attempt to achieve efficiently and expeditiously its objectives described in the Program of Research attached to this Agreement pursuant to Section 2.2.2.

4.2.4 IDENTIFICATION OF NOVEL VALIDATED TARGETS. Novartis shall notify the CMC in writing of any Novel Validated Targets identified by Novartis during the Research Period of each At-Novartis Project promptly after its identification. Such notice shall be accompanied with a report and sufficient data which establish that the validation criteria predetermined pursuant to Section 2.2.2(d) have been met. CMC shall issue a list of the Novel Validated Targets identified in the course of such At-Novartis Project as a part of the minutes of each CMC meeting and a final list within thirty (30) days after the end of such Research Period. The date on which Novartis has provided the notice described in this Section 4.2.4 shall be considered the "Notice Date" of such Novel Validated Target.

4.2.5 TECHNOLOGY TRANSFER. Rigel will transfer to Novartis such Rigel Technology and Rigel Core Technology, including without limitation the Phoenix packaging cell line, as reasonably necessary to enable the target identification activities Novartis is to perform in each At-Novartis Project as proposed by Novartis and reasonably acceptable to Rigel; provided, however, that Novartis shall reimburse Rigel its reasonable costs and expenses therefor. Novartis may use such Rigel Technology and Rigel Core Technology pursuant to the licenses granted under this Agreement.

4.3 ADDITIONAL PROJECTS. If Novartis expresses an interest in cooperating with Rigel with respect to any Programs of Research in addition to the two Joint Projects and three At-Novartis Projects, Rigel and Novartis will meet promptly to discuss in good faith whether and under what terms they could agree to cooperate with respect to such further research projects.

4.4 DISCLOSURE. Rigel and Novartis will disclose to the CMC promptly and at least quarterly the results of the research activities conducted in each Collaboration Project, such reports to be in such form as specified by the CMC. The Parties shall keep complete and accurate records pertaining to the results of work conducted pursuant to each Collaboration Project. Such records shall be maintained by each Party for a period of at least three (3) years following the year in which any such efforts were made hereunder.

4.5 DISCRETIONARY TERMINATION OF RESEARCH PERIOD.

4.5.1 DISCRETIONARY TERMINATION DATE FOR JOINT PROJECTS. Novartis may at its discretion terminate each Joint Project, individually, upon at least six (6) months prior written notice as hereinafter provided. If Novartis gives notice of termination for a given Joint Project no later than eighteen (18) months from the applicable Commencement Date, termination of such Joint Project will take effect at twenty-four (24) months from its Commencement Date. If Novartis gives notice of termination for a given Joint Project after eighteen (18) months but no later than thirty-six (36) months from the applicable Commencement Date, termination of such Joint Project will take effect at forty-two (42) months from its Commencement Date.

4.5.2 DISCRETIONARY TERMINATION OF AT-NOVARTIS PROJECTS. Novartis may, at its discretion, terminate each At-Novartis Project, individually, at any time with immediate effect.

4.5.3 EFFECT OF DISCRETIONARY TERMINATION.

(a) If Novartis terminates the T-Cell Project effective twenty-four (24) months after the applicable Commencement Date or forty-two (42) months after the applicable Commencement Date, Novartis will keep all rights and licenses granted under Section 6.2 with respect to those Novel Validated Targets identified prior to the termination of the Research Period, subject to the applicable milestone and/or royalty payment obligations of Article 7 and Exhibit C.

(b) If Novartis terminates any Joint Project other than the T-Cell Project

(i) effective twenty-four (24) months after the applicable Commencement Date, all licenses granted to Novartis relating to such Joint Project shall terminate upon the termination such Joint Project, and the rights to all Novel Validated Targets identified as of the date of termination shall revert to Rigel;

(ii) effective forty-two (42) months from the applicable Commencement Date, Novartis will keep all rights and licenses granted under Section 6.2 with respect to those Novel Validated Targets identified prior to the termination of the Research Period, subject to the applicable milestone and/or royalty payment obligations of Article 7 and Exhibit C.

(c) If Novartis terminates any At-Novartis Project at or effective prior to forty-two (42) months after the applicable Commencement Date, all licenses granted to Novartis relating to such At-Novartis Project shall terminate upon termination of such At-Novartis Project, and the rights to all Novel Validated Targets identified as of the date of termination shall revert to Rigel. If Novartis terminates an At-Novartis Project after forty-two (42) months, Novartis shall keep the rights to the Novel Validated Targets identified in the course of such At-Novartis Project as licensed under Section 6.2.

4.6 TERMINATION OF COLLABORATION PROJECT FOR BREACH.

4.6.1 Either Party may terminate a Collaboration Project after sixty (60) days prior notice to the other that the other Party has committed a material breach of its obligations

in the performance of such Collaboration Project unless the other Party cures (to the extent practicable) the breach within such period of time.

4.6.2 If Novartis terminates a Collaboration Project under Section 4.6.1 above, Novartis will keep all rights and licenses granted under Section 6.2 with respect to those Novel Validated Targets identified prior to the termination of the Research Period, subject to the applicable milestone and/or royalty payment obligations of Article 7 and Exhibit C.

4.6.3 If Rigel terminates a Collaboration Project under Section 4.6.1 above, all licenses granted to Novartis for such Collaboration Project shall terminate and the rights to all Novel Validated Targets identified

in the course of such Collaboration Project shall revert to Rigel.

4.7 TERMINATION OF JOINT PROJECT FOR SCIENTIFIC REASONS. If it is determined by both Parties before the end of the 12th month of a Joint Project already underway that it is no longer scientifically feasible, the Parties shall meet for good faith discussions to determine if an alternate project may be substituted on substantially similar terms. If after the 12th month of a Joint Project the CMC determines that for scientific reasons, a Joint Project cannot yield any Novel Validated Targets, or that such Novel Validated Targets will not be suitable for Compound Screening in high-throughput format, Novartis shall have to right to terminate such Joint Project with written notice effective upon receipt by Rigel. Upon such termination, Novartis shall make to Rigel, upon receipt of a corresponding invoice, a termination payment for non-cancelable commitments and other costs incurred by Rigel due to such termination corresponding to three (3) months of the research support payable pursuant to Section 7.1. Upon termination pursuant to this Section 4.7, all licenses granted to Novartis for such Joint Project shall terminate, and the rights to all Novel Validated Targets identified in the course of such Joint Project (if any) shall revert to Rigel.

4.8 EXISTING OBLIGATIONS. The termination of any Research Period shall not relieve the Parties of any obligation that accrued prior to such expiration or termination.

5. COMPOUND SCREENING AND DEVELOPMENT

5.1 NOVARTIS COMPOUND SCREENING. Novartis shall have the right to initiate Compound Screening with each Novel Validated Target upon notice to Rigel any time during the Exclusivity Term with respect to such Novel Validated Target.

5.2 EXCLUSIVITY TERM. Novartis' screening right under Section 5.1 shall be exclusive ('exclusive', as used in this Section 5.2 and subject to the provisions of Section 5.5, shall mean 'to the exclusion also of Rigel') during the first two (2) years ("Exclusivity Term") after the Notice Date. Subject to Section 5.3, Novartis may, after the first two years, extend the Exclusivity Term with respect to a Novel Validated Target for up to five (5) additional one (1) year periods upon payment to Rigel of the appropriate Extension Fee provided in Section 7.5 on or before (i) the day which is thirty (30) days prior to the end of such Exclusivity Term or (ii) if Novartis has informed Rigel in writing on or before a date with is sixty (60) days prior to the end of such Exclusivity Term, thirty (30) days after receipt of a corresponding invoice from Rigel, whichever is the later. Upon expiration of the Exclusivity Term, Novartis' right to conduct Compound Screening with a Novel Validated Target, subject to the payments required by Section 7.2 and 7.4, shall become nonexclusive

and Rigel shall also have the nonexclusive right, including the right to sublicense, to conduct Compound Screening with such Novel Validated Target.

5.3 NOVARTIS DILIGENCE.

5.3.1 In addition to the payment of the Extension Fee and as a further condition for Novartis to extend the Exclusivity Term, Novartis shall be obligated to maintain itself or through its Affiliates or sublicensees a diligent, continuous program of utilizing the Novel Validated Target to identify molecules useful for the development and manufacture of Products.

5.3.2 Novartis shall be deemed to be maintaining a diligent continuous program with respect to a Novel Validated Target if Novartis (i) is actively using the Novel Validated Target in Novartis' screening systems for Compound Screening or, (ii) is actively undertaking diligent, commercially reasonable efforts, similar to those used for products of comparable commercial potential originating in Novartis for the continuing development of a Product and the commercialization of a Product including, without limitation, the performance of an active derivatisation and lead optimization program, the designation of FSC Status, initiation of clinical trials, submission of regulatory filings and commercial launch of a Product.

5.4 REPORTING. During each applicable Exclusivity Term, Novartis shall provide information on its activities under Section 5.3.1 or 5.3.2 above to the CMC on a quarterly basis. At any time during the Exclusivity Term with respect to a Novel Validated Target, Novartis shall on a not less than quarterly basis provide documentation to the reasonable satisfaction of Rigel that Novartis is maintaining a diligent, continuous program with respect to the Novel Validated Target.

5.5 CONVERSION OF EXCLUSIVE RIGHT. If Novartis does not pay the Extension Fee or does not maintain a diligent continuous program with respect to a Novel Validated Target as provided in Section 5.3 above, then the Exclusivity Term shall be deemed expired and Novartis' screening right under Section 5.1, subject to the payments required by Section 7.2 and 7.4, shall become non-exclusive, perpetual, and fully paid-up, and Rigel shall have the

nonexclusive right, including the right to sublicense, to conduct Compound Screening with such Novel Validated Target.

5.6 RIGEL SCREENING. At any time during the Exclusivity Term with respect to a Novel Validated Target, Novartis, at its sole discretion, may request in writing that Rigel conduct Compound Screening of Rigel's small-molecule compound library against such Novel Validated Target. If Rigel agrees to conduct such screening, the CMC shall establish criteria for an active compound to qualify as a Lead Compound. Thereafter, Rigel will conduct such screening pursuant to a workplan to be agreed to by the Parties. If Rigel identifies a Lead Compound, it shall so notify Novartis, and Section 6.4 hereof shall then apply.

6. LICENSE GRANTS; NONCOMPETITION

6.1 RESEARCH LICENSE GRANTS.

6.1.1 GRANT BY RIGEL. Rigel hereby grants to Novartis and its Affiliates a nonexclusive, non-transferable, royalty-free license during the Research Period for each

Collaboration Project under the Rigel Technology, Rigel Core Technology and Rigel's interest in Project Technology in the Territory, subject to the terms of this Agreement, solely for the purpose of carrying out Novartis' responsibilities under the applicable Collaboration Project.

6.1.2 GRANT BY NOVARTIS. Novartis hereby grants to Rigel and its Affiliates a nonexclusive, non-transferable, royalty-free license during the Research Period for each Collaboration Project under the Novartis Technology and Novartis' interest in the Project Technology, subject to the terms of this Agreement, solely for the purpose of carrying out Rigel's responsibilities under the applicable Collaboration Project.

6.2 COMMERCIAL LICENSE GRANTS.

6.2.1 Subject to Section 5.3 and the other terms and conditions of this Agreement, Rigel hereby grants to Novartis and its Affiliates an exclusive license, with the right to grant sublicenses, under the Rigel Technology and Rigel's interest in the Project Technology to make, have made, use, import, offer for sale and sell Products.

6.2.2 Subject to the terms and conditions of this Agreement, Rigel hereby grants to Novartis and its Affiliates a nonexclusive, non-transferable, royalty-free license under Rigel Core Technology only for confirmational screening and similar uses relating to Novel Validated Targets identified in the course of a Collaboration Project, it being understood that Novartis has the right to use such Technology for the purposes of further development, registration and commercialisation of Products.

6.3 LICENSE TO RIGEL OF IMPROVEMENTS TO RIGEL CORE TECHNOLOGY. Novartis hereby grants to Rigel a nonexclusive, royalty-free, worldwide license, with the right to sublicense, under Novartis' interest in the Project Technology only to the extent it constitutes an improvement of the Rigel Core Technology licensed to Novartis hereunder. For the avoidance of any doubt, the license granted by Novartis under this Section 6.3 shall not include, without limitation, any Patents or Know-How claiming the composition of matter, method of making or use of Products.

6.4 OPTION FOR LICENSE FOR RIGEL LEAD COMPOUND. Novartis shall have an option during the ninety (90) days following receipt of Rigel's notice of identification of a Lead Compound as provided in Section 5.6 to negotiate with Rigel a worldwide, exclusive license to such Lead Compound and compounds derived therefrom under terms to be agreed but including those shown on Exhibit C hereto. If Novartis does not execute such a license within such period, Rigel shall have no further obligation or liability to Novartis for such Lead Compound.

7. FINANCIAL SUPPORT

7.1 RESEARCH SUPPORT. Novartis will provide funding to support Rigel's efforts during the Research Period of each Joint Project, on an FTE basis at a rate of $250,000 per year multiplied by the number of FTEs as shown in Exhibit B for such Joint Project. The amounts payable shall be paid in advance by certified or bank check or wire transfer in United States dollars in four equal payments to be paid quarterly upon presentation of a corresponding invoice by Rigel. Payments shall be made no later than (a) by the first (1st) business day of each applicable Research Period quarter or (b) thirty (30) days after receipt of the

corresponding invoice, whichever is the later. Research support under this Section 7.1 shall not be credited against any equity, milestone or royalty payments due Rigel hereunder.

7.2 MILESTONE PAYMENTS TO RIGEL. Novartis will pay to Rigel the following amounts ("Milestone Payments") in respect of the achievements with respect to each Joint Project and each At-Novartis Project:

<TABLE>
<CAPTION>

MILESTONE EVENT		AMOUNT OF PAYMENT
<S>		<C>
1)	NOTICE DATE OF THE FIRST NOVEL VALIDATED TARGET	$500,000
2)	NOTICE DATE OF EACH SUBSEQUENT NOVEL VALIDATED TARGET - PER NOVEL VALIDATED TARGET	$250,000
3)	INITIATION OF COMPOUND SCREENING WITH EACH NOVEL VALIDATED TARGET:	
	PER NOVEL VALIDATED TARGET:	
	FIRST FOUR (4) NOVEL VALIDATED TARGETS, CUMULATED OVER ALL COLLABORATION PROJECTS	$1.25 million
	EACH SUBSEQUENT NOVEL VALIDATED TARGET	$1 million
4)	FSC STATUS DECLARATION OF THE FIRST PRODUCT IDENTIFIED IN COMPOUND SCREENING CONDUCTED AGAINST EACH NOVEL VALIDATED TARGET PURSUANT TO SECTION 5.3 - PER NOVEL VALIDATED TARGET	$1.5 million
5)	FIRST PRODUCT IDENTIFIED ON THE BASIS OF A NOVEL VALIDATED TARGET ENTERS PHASE I CLINICAL TRIALS - PER NOVEL VALIDATED TARGET	$2.5 million

</TABLE>

All Milestone Payments to be made by Novartis to Rigel pursuant to this Section 7.2 shall be made within thirty (30) days of receipt of an invoice from Rigel. Novartis shall promptly report to Rigel the occurrence of the Milestone Events 3), 4), and 5).

7.3 PROJECT ACCESS PAYMENTS. No later than (a) by the Commencement Date of each Joint Project and each At-Novartis Project or (b) thirty (30) days after receipt of the corresponding invoice from Rigel, whichever is the later, Novartis will pay Rigel a project access fee of $400,000.

7.4 ROYALTIES. Novartis shall pay to Rigel all royalties due to Third Party licenses listed on Exhibit D hereto in the event Novartis shall practice the inventions of the Patents licensed thereunder. Further, if applicable pursuant to Articles 5.6 and 6.4, Novartis shall pay to Rigel the royalties as provided in Exhibit C. For the avoidance of any doubt, Novartis shall pay to Rigel no other royalties under this Agreement.

7.5 EXTENSION FEE. As provided in Section 5.2, the amount payable by Novartis to extend the Exclusivity Term for each year after the initial two (2) year Exclusivity Term

for a Novel Validated Target ("Extension Fee") shall be $50,000 for the third (3rd) year, $100,000 for the fourth (4th) year and, $200,000 for each of the fifth (5th), sixth (6th) and seventh (7th) year.

8. INTELLECTUAL PROPERTY

8.1 OWNERSHIP OF PROJECT KNOW-HOW; INVENTIONS. Project Know-How invented (as determined in accordance with United States rules of inventorship) solely by employees of one Party during the course of a Collaboration Project ("Sole Inventions") shall be the property of such Party. In the event that employees of Novartis and Rigel jointly invent any Project Know-How (again as determined in accordance with United States rules of inventorship), such Project Know-How shall be owned jointly by Novartis and Rigel, each to own an undivided one-half (1/2) interest in such Project Know-How ("Joint Invention") except as provided herein. Each Party shall cooperate with the other in completing any patent applications relating to Joint Inventions, and in executing and delivering any instrument required to assign, convey or transfer to such other Party its undivided one-half (1/2) interest.

8.2 PATENT PROSECUTION.

8.2.1 Novartis Patents and Rigel Patents licensed hereunder

shall be prosecuted and maintained by Novartis and Rigel, respectively, at such Party's option and its own expense; provided, however, that the Parties shall consult with and consider the comments of the CMC with respect to the prosecution of applications for such patents.

8.2.2 Each Party will prepare, file, prosecute and maintain patent applications for its Sole Inventions and shall be responsible for related interference proceedings.

8.2.3 In case of Joint Inventions, the Parties will mutually agree on the responsibility for filing and prosecuting applications or patent applications relating thereto, and the defense against Third Parties who infringe on Patents issuing thereon.

8.3 INFRINGEMENT OF THIRD-PARTY RIGHTS.

8.3.1 If a Third Party claims that the practice of the Rigel Technology or Rigel Core Technology under this Agreement infringes on its Patents, each Party shall notify the other Party promptly upon learning of such claim.

8.3.2 Promptly upon such notification, the Parties shall meet to discuss the strategy and appropriate steps to be taken to deal with such claim, including, without limitation, by working around the Patents of the Third Party, by practicing the Rigel Technology or Rigel Core Technology in countries where the Third Party has no applicable Patents, by seeking to invalidate the Third Party Patents or by entering into negotiations with such Third Party regarding a license under its Patents. The Parties shall further agree on an equitable and fair distribution of the costs resulting from any such course of action.

9. REPRESENTATIONS AND WARRANTIES

9.1 REPRESENTATIONS AND WARRANTIES. Each Party represents and warrants to the other that:

9.1.1 CORPORATE POWER. It is duly organized and validly existing under the laws of its state or country of incorporation, and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof.

9.1.2 DUE AUTHORIZATION. It is duly authorized to execute and deliver this Agreement and to perform its obligations hereunder, and the person or persons executing this Agreement on its behalf has been duly authorized to do so by all requisite corporate action.

9.1.3 BINDING AGREEMENT. This Agreement is legally binding upon it and enforceable in accordance with its terms. The execution, delivery and performance of this Agreement by it does not conflict with any agreement, instrument or understanding, oral or written, to which it is a party or by which it may be bound, nor violate any material law or regulation of any court, governmental body or administrative or other agency having jurisdiction over it.

9.1.4 GRANT OF RIGHTS; MAINTENANCE OF AGREEMENTS. It has not, and will not during the Term of the Agreement, grant any right to any Third Party which would conflict with the rights granted to the other Party hereunder. It has (or will have at the time performance is due) maintained and will maintain and keep in full force and effect all agreements necessary to perform its obligations hereunder.

9.1.5 VALIDITY. It is aware of no action, suit or inquiry or investigation instituted by any governmental agency which questions or threatens the validity of this Agreement.

9.1.6 EMPLOYEE OBLIGATIONS. All of its employees, officers and consultants have executed agreements requiring in the case of employees and officers, assignment to the Party of all inventions made during the course of and as a result of their association with such Party and obligating the individual to maintain as confidential the confidential information of the Party, as well as the confidential information of a Third Party which such Party may receive.

9.2 DISCLAIMER CONCERNING TECHNOLOGY. THE TECHNOLOGY PROVIDED BY EACH PARTY HEREUNDER IS PROVIDED "AS IS" AND EACH PARTY EXPRESSLY DISCLAIMS ANY AND ALL WARRANTIES OF ANY KIND, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION THE WARRANTIES OF DESIGN, MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, NONINFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES OR ARISING FROM A COURSE OF DEALING, USAGE OR TRADE PRACTICES, IN ALL CASES WITH RESPECT THERETO. Without limiting the generality of the foregoing, each Party expressly does not warrant (i) the success of any Program of Research or (ii) the safety or usefulness for any purpose of the technology it provides

hereunder.

10. CONFIDENTIALITY; PUBLICATION

10.1 CONFIDENTIALITY. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing by the Parties, the Parties agree that, for the Term of the Agreement and for five (5) years thereafter, the receiving Party (the "Receiving Party") shall keep confidential and shall not publish or otherwise disclose and shall not use for any purpose other than as provided in this Agreement any Confidential Information furnished to it

by the other Party (the "Disclosing Party") pursuant to this Agreement unless the Receiving Party can demonstrate by contemporaneous, competent written proof that such Confidential Information:

(a) was already known to the Receiving Party, other than under an obligation of confidentiality, at the time of disclosure by the Disclosing Party;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the Receiving Party in breach of the Agreement;

(d) was disclosed to the Receiving Party, other than under an obligation of confidentiality to a Third Party, by a Third Party who had no obligation to the Disclosing Party or any Third Party not to disclose such information to others; or

(e) was independently discovered or developed by the Receiving Party without the use of Confidential Information belonging to the Disclosing Party.

10.2 AUTHORIZED DISCLOSURE.

10.2.1 Each Party may disclose Confidential Information belonging to the other Party to the extent such disclosure is reasonably necessary in the following instances:

(a) filing or prosecuting Patents relating to Project Know-How;

(b) regulatory filings;

(c) prosecuting or defending litigation;

(d) complying with applicable governmental regulations;

(e) conducting pre-clinical or clinical trials of Products; and

(f) disclosure to Affiliates, sublicensees, employees, consultants or agents who agree to be bound by similar terms of confidentiality and non-use at least equivalent in scope to those set forth in this Article 10.

10.2.2 Notwithstanding the foregoing, in the event a Party is required to make a disclosure of the other Party's Confidential Information pursuant to this Section 10.2 it will, except where impracticable, give reasonable advance notice to the other Party of such disclosure and use commercially reasonable efforts to secure confidential treatment of such information. In any event, the Parties agree to take all reasonable action to avoid disclosure of Confidential Information hereunder. The Parties will consult with each other and agree on the provisions of this Agreement to be redacted in any filings made by the Parties with the Securities and Exchange Commission or as otherwise required by law.

10.3 PUBLICATIONS.

10.3.1 REVIEW AND APPROVAL. Each Party to this Agreement recognizes that the publication of papers, including oral presentations and abstracts, regarding the Research Cooperation, subject to reasonable controls to protect Confidential Information, can be beneficial to both Parties. However, each Party shall have the right to review and approve any paper proposed for publication by the other Party, including oral presentations and abstracts,

which utilizes data generated from the Research Cooperation or includes Confidential Information of the reviewing Party.

10.3.2 REVIEW AND APPROVAL PROCESS. At least forty-five (45) days before any such paper is presented or submitted for publication, the Party proposing publication shall deliver a complete copy to the other Party. The receiving Party shall review any such paper and give its comments to the publishing Party within thirty (30) days of the delivery of such paper to the receiving Party. With respect to oral presentation materials and abstracts, the Parties shall make reasonable efforts to expedite review of such materials and abstracts, and shall return such items as soon as practicable to the publishing Party with appropriate comments, if any, but in no event later than thirty (30) days from the delivery date thereof to the receiving Party. The publishing Party shall comply with the other Party's request to delete references to such other Party's Confidential Information in any such paper and agrees to withhold publication of same an additional ninety (90) days in order to permit the Parties to obtain patent protection, if either of the Parties deem it necessary, in accordance with the terms of this Agreement.

10.4 SAMPLES. Samples of compounds provided by one Party (the "Supplying Party") to the other Party (the "Receiving Party") during the Research Program shall not be supplied or sent by the Receiving Party to any Third Party without the written consent of the Supplying Party. The Receiving Party shall return to the Supplying Party any samples not used upon expiration or termination of the applicable Research Period, except that Novartis may retain such samples to the extent necessary to exercise the licenses granted in Section 6.2.

11. TERM AND TERMINATION

11.1 TERM OF THE AGREEMENT. This Agreement shall become effective upon the Effective Date and continue until the later of (i) the expiration of the obligation of Novartis to pay royalties as provided in Section 7.4, and (ii) the expiration of the last Patent licensed to Novartis under this Agreement, whereupon the licenses granted under Sections 6.2 and 6.3 shall be deemed non-exclusive, perpetual and fully paid-up.

11.2 TERMINATION FOR MATERIAL BREACH. Each Party shall have the right to terminate this Agreement after ninety (90) days prior notice to the other that the other Party has committed a material breach of the Agreement other than performance of obligations under a Collaboration Project, unless the other Party cures (to the extent practicable) the breach within such period of time. Licenses granted to the non-breaching Party under Section 6 of this Agreement shall not be affected by termination for material breach. All licenses granted to the breaching Party under Section 6 of this Agreement shall automatically terminate upon such termination.

11.3 ACCRUED RIGHTS, SURVIVING OBLIGATIONS. Expiration or termination of this Agreement shall not affect any accrued rights or obligations of either Party. Sections 9, 10, 11 (and Section 6 to the extent referenced therein), 12, 13, 14.1, and 14.3 through 14.10, and any

definitions of terms used therein shall survive any expiration or termination of this Agreement.

12. INDEMNITY

12.1 INDEMNIFICATION. Each Party hereby agrees to save, defend and hold the other Party and its directors, officers, employees, and agents harmless from and against any and all claims, suits, actions, demands, liabilities, expenses and/or loss, including reasonable legal expense and attorneys' fees (collectively, "Claims") for damage to persons or property resulting directly or indirectly from actions in connection with a Collaboration Project by the indemnifying Party, its Affiliates, agents or sublicensees, but only to the extent such Claims result from the gross negligence or willful misconduct of the indemnifying Party or its Affiliates, agents or sublicensees and do not result from the negligence of the Party seeking indemnification.

12.2 PRODUCT LIABILITY. Novartis hereby agrees to indemnify, hold harmless and defend Rigel and its directors, officers, employees, and agents against any Claim or Claims, including, but not limited to claims for bodily injury and death, resulting from or arising out of the manufacture, use or sale of Products by Novartis, its Affiliates and sublicensees.

12.3 CONTROL OF DEFENSE. Any entity entitled to indemnification under this Article 12 shall give notice to the indemnifying Party of any Claims that may be subject to indemnification and, promptly after learning of such Claim, the indemnifying Party shall assume the defense of such Claims with counsel reasonably satisfactory to the indemnified Party. If such defense is assumed by the indemnifying Party with counsel so selected, the indemnifying Party will not be subject to any liability for any settlement of such Claims made by the indemnified Party without its consent (but such consent will not be unreasonably

withheld or delayed), and will not be obligated to pay the fees and expenses of any separate counsel retained by the indemnified Party with respect to such Claims.

13. GOVERNING LAW; DISPUTE RESOLUTION

13.1 GOVERNING LAW. This Agreement shall be governed by laws of the state of Delaware, as such law applies to contracts entered into in Delaware by residents of Delaware, without reference to its choice of law provisions.

13.2 DISPUTE RESOLUTION. In the event of any dispute, the Parties shall refer such dispute to a designated executive of Rigel and a designated executive of Novartis for attempted resolution by good faith negotiations within thirty (30) days after such referral is made. In the event such executives are unable to resolve such dispute within such thirty (30) day period, either Party may invoke the provisions of Section 13.3 below.

13.3 JURISDICTION AND VENUE. Except as provided in Section 13.2 above, any claim or controversy arising out of or related to this Agreement or any breach hereof shall be adjudicated in the federal district court of Dover, Delaware, and the Parties hereby consent to the jurisdiction and venue of such court.

14. GENERAL PROVISIONS

14.1 NOTICES. All notices required or permitted to be given under this Agreement shall be in writing and shall be mailed by registered or certified mail addressed to

the signatory to whom such notice is required or permitted to be given and transmitted by facsimile to the number indicated below. All notices shall be deemed to have been given when mailed, as evidenced by the postmark at the point of mailing, or faxed; provided that such fax is confirmed by electronic confirmation of transmission.

All notices to Novartis shall be addressed as follows:

Novartis Pharma AG
Lichtstrasse 35
P.O. Box
CH-4002 Basel
Switzerland
Attn: Legal Department
Fax: +41-61-324-6859

All notices to Rigel shall be addressed as follows:

Rigel Pharmaceuticals, Inc.
240 East Grand Avenue
South San Francisco, CA 94080
Attn: President
Fax: +1-650-624-1101

with a copy to:

Cooley Godward LLP
Five Palo Alto Square
3000 El Camino Real
Palo Alto, California 94306
Attn: Patrick A. Pohlen, Esq.
Fax: (650) 857-0663

Any Party may, by written notice to the other, designate a new address or fax number to which notices to the Party giving the notice shall thereafter be mailed or faxed.

14.2 FORCE MAJEURE. No Party shall be liable for any delay or failure of performance to the extent such delay or failure is caused by circumstances beyond its reasonable control and that by the exercise of due diligence it is unable to prevent, provided that the Party claiming excuse uses commercially reasonable efforts to overcome the same.

14.3 ENTIRETY OF AGREEMENT. This Agreement embodies the entire, final and complete agreement and understanding between the Parties and replaces and supersedes all prior discussions and agreements between them with respect to its subject matter. No modification or waiver of any terms or conditions hereof shall be effective unless made in writing and signed by a duly authorized officer of each Party.

14.4 NON-WAIVER. The failure of a Party in any one or more instances to insist upon strict performance of any of the terms and conditions of this Agreement shall not constitute a waiver or relinquishment, to any extent, of the

right to assert or rely upon any such terms or conditions on any future occasion.

14.5 DISCLAIMER OF AGENCY. Neither Party is, or will be deemed to be, the legal representative or agent of the other, nor shall either Party have the right or authority to assume, create, or incur any third Party liability or obligation of any kind, express or implied, against or in the name of or on behalf of another except as expressly set forth in this Agreement.

14.6 SEVERABILITY. If a court of competent jurisdiction declares any provision of this Agreement invalid or unenforceable, or if any government or other agency having jurisdiction over either Rigel or Novartis deems any provision to be contrary to any laws, then that provision shall be severed and the remainder of the Agreement shall continue in full force and effect. To the extent possible, the Parties shall revise such invalidated provision in a manner that will closely approximate the Parties' original intent.

14.7 AMBIGUITIES. The Parties hereby acknowledge that they have drafted this Agreement jointly. Thus, any presumption that ambiguous provisions shall be construed against the party drafting an agreement is inapplicable, and each Party expressly agrees not to invoke said presumption in the event of a dispute between the Parties relating to this Agreement.

14.8 AFFILIATES; ASSIGNMENT. Except as otherwise provided herein, neither Party may assign its rights or delegate its duties under this Agreement without the prior written consent of the other Party, not to be unreasonably withheld; provided, however, that either Party may assign this Agreement to any of its Affiliates or to any successor by merger or sale of substantially all of the assets or business unit to which this Agreement relates; provided further, however, that any such assignment shall be made in a manner such that the assignee expressly undertakes in writing to be liable and responsible for the performance and observance of all its duties and obligations hereunder. This Agreement shall be binding upon the successors and permitted assigns of the Parties. Any attempted delegation or assignment not in accordance with this Section 14.7 shall be of no force or effect.

14.9 HEADINGS. The headings contained in this Agreement have been added for convenience only and shall not be construed as limiting.

14.10 COUNTERPARTS. This Agreement may be executed in one or more counterparts, each of which shall be an original and all of which shall constitute together the same document.

IN WITNESS WHEREOF, the Parties hereto have duly executed this Agreement.

RIGEL PHARMACEUTICALS, INC.	NOVARTIS PHARMA AG
By: /s/ James M. Gower	By: /s/ Paul Herring
Name: James M. Gower	Name: Dr. Paul Herring
Title: President & CEO	Title: Head of Research

EXHIBIT A-1

T-CELL PROGRAM OF RESEARCH

NOVEL REGULATORY PATHWAYS IN T AND B LYMPHOCYTES

NOVARTIS PROJECT OUTLINE

PROJECT I: IDENTIFICATION OF REGULATORY PROTEINS THAT AFFECT T CELL ACTIVATION

INTRODUCTION

Activation of specific signaling pathways in lymphocytes determines the quality, magnitude and duration of immune responses. In transplantation, acute and chronic inflammatory diseases, and autoimmunity, it is these pathways that are responsible for the induction, maintenance and exacerbation of disease lymphocyte responses. Of the many activation pathways that have been elucidated, most are ubiquitous and not unique to a particular cell lineage. The goal of this proposal is to identify and validate novel signaling molecules specific for T cell activation and effector function. From these molecules, T cell-specific targets will be identified that are effective in modulating immune-mediated processes. A combination of high throughput functional and yeast two-hybrid genetic screens will be employed to isolate and map novel signaling molecules in lymphocyte activation. Engagement of the B cell receptor (BCR) in conjunction with T cell assistance stimulates humoral immunity characterized by immunoglobulin production and antigen presentation by B cells. Likewise, T cell signaling through the T cell receptor (TCR) and other molecules such as CD28 leads to specific cellular immunity. Summarized below, in Table 1, is our strategy for identifying and validating novel T cell intracellular signaling molecules. Each approach, its readout, and the libraries to be used are detailed in the remaining sections of the proposal.

TABLE 1. SUMMARY OF SCREENS TO IDENTIFY INTRACELLULAR REGULATORS OF LYMPHOCYTE ACTIVATION AND/OR EFFECTOR FUNCTION.

<TABLE>
<CAPTION>

APPROACH	READOUT	INTRACELLULAR TARGETING STRUCTURES AND MOTIFS
<S> PROJECT I IDENTIFICATION OF REGULATORY PROTEINS THAT AFFECT T CELL ACTIVATION	<C>	<C>
1. PRIMARY SCREENS		
1.1 Primary peptide screen for inhibition of CD25 (IL-2R(alpha) chain) in a cell line (to be determined by the RMC) stimulated through CD3 +/-CD28	Enrichment by FACS for absent or decreased CD25 expression (measured by (alpha) -CD25 monoclonal antibody) Enrichment by FACS for absent or decreased reporter activity (fluorescence-based screen) or isolation of survivors (survival-based screen)	GFP/BFP scaffold peptide libraries (12 mer and 18 mer) Potential additional library scaffolds (constrained 18 mer (beta)- lactamase, DHFR) to be determined by the RMC
1.2 Primary peptide screen for inhibition of IL-2 promoter activity in a cell line stimulated through CD3 +/-CD28		
2. SECONDARY ASSAYS		
2.1 Secondary assays measuring expression of cell surface T cell co-stimulatory molecules in T cell lines (to be determined by the RMC) and primary human PBL T cells stimulated through CD3 +/-CD28	Analytical flow cytometry measuring expression of CD28, CTLA-4, ICOS, CDw150 and CD40L (additional markers to be determined by the RMC) Analytical flow cytometry measuring expression of Th1/Th2 differentiation markers to be determined by the RMC (e.g., (beta) subunits of IL-12 and IFN(gamma) receptors, ESTE-2, IL-12R(alpha), CD45RA, CD45RO and CD148)	
2.2 Secondary assays measuring T cell differentiation into Th1 and Th2 cells in T cell lines (to be determined by the RMC) and primary human PBL T cells; stimulus to be determined by the RMC		
3. PATHWAY MAPPING		
3.1 Yeast two-hybrid screens on cDNA and peptide hits to identify intracellular binding	Lac Z+, His	cDNA: -Anti-CD3 activated T cells from human spleen

partners; functional
analysis of interacting
proteins

3.2 Yeast-Two Hybrid isolation of peptides that bind to functional cDNAs;	Lac Z+, His+	Constrained 18 mer and other scaffolds (GFP/BFP, (beta)-lactamase, DHFR) to be
functional analysis of these peptides		determined by the RMC

</TABLE>

2.

<TABLE>
<S> <C> <C>

PROJECT I.

IDENTIFICATION OF REGULATORY PROTEINS THAT AFFECT T CELL ACTIVATION.

1 Primary Screens

Screens in Project I will isolate inhibitors/modulators of TCR-induced T cell activation (Appendix A). CD25 and IL-2 are such fundamental markers of activated T cells that their upstream regulators may also be biased toward T cell co-stimulation and/or Thl/2 development. Blockade of the above markers will negatively affect T cell function and B-T cell interactions leading to T cell activation. Modulating T cell activation and function has clinical relevance for transplantation, autoimmunity and inflammatory diseases.

1.1 Primary peptide screen for inhibition of CD25 in T cells stimulated through CD3 +/-CD28

CD3 positive T cell lines will be selected for their ability to upregulate CD25 and produce IL-2 in response to crosslinking of their TCR. The cell lines selected for primary screening will possess kinetics and levels of expression of the above markers that are most similar to primary human peripheral blood and splenic T cells. In primary screens, CD25 will be measured by flow cytometry and enriched for desired phenotypes following peptide library expression. The T cell lines will each be infected with 4 peptide libraries: two loop-3 BFP scaffold peptide libraries (12 mer and 18 mer) and two loop-4 BFP scaffold peptide libraries (12 mer and 18 mer. Other library scaffolds may be utilized as deemed necessary by the RMC (constrained 18 mer, (beta)-lactamase, DHFR). After several rounds of enrichment, individual peptide sequences will be tested for function in the original screening assay.

1.2 Functional screening for inhibitors of TCR-induced transcription of the IL-2 promoter in cell lines carrying the IL-2 promoter upstream of a reporter fused to death genes.

An alternative method for the flow-based screen described in section 1.1 is to generate cell lines that monitor IL-2 promoter activity by survival. A CD3-responsive fragment of the IL-2 promoter will be cloned into a retroviral vector in the reverse orientation. This will be upstream of a splice site followed by a reporter (GFP) and then an IRES ending with a fusion of two death genes, thymidine kinase (TK) and cytosine deaminase (CD) (Appendix B). This construct will be packaged and used to infect the CD3-responsive T cell lines. In response to activation of the IL-2 promoter, the infected cells will become fluorescent or, after addition of the death ligand (ganciclovir for TK and 5-FC (fluorocytosine) for CD), will die. These reporter/survival T cell lines will be infected with 4 libraries: two loop-3 BFP scaffold peptide libraries (12 mer and 18 mer) and two loop-4 BFP scaffold peptide libraries (12 mer and 18 mer). Other library scaffolds may be utilized as deemed necessary by the RMC (constrained 18 mer, (beta) lactamase, DHFR). Peptides capable of inhibiting promoter activity will decrease GFP expression. Peptides capable of shutting off the promoter will rescue the cells from death in the presence of the death gene inducers. After sufficient rounds of enrichment, individual peptide sequences will be tested for function in the original screening assay. This reporter/survival strategy is adaptable to any promoter that is inducible by an extracellular signal. As proof of principle, we have generated cell lines expressing TK,

3.

CD8/CD95 and TK/GFP fusion that are efficiently killed in the presence of ganciclovir or anti-CD8 monoclonal antibody, respectively (Appendix C).

2. SECONDARY ASSAYS

2.1 Secondary assays measuring expression of cell surface T cell co-stimulatory molecules in T cell lines and primary human PBL T cells stimulated through CD3 +/-CD28

Confirmed peptide hits from the primary functional screens will be subjected to secondary assays in T cell lines and primary peripheral blood and splenic T cells. In these assays, the effects of the hits on CD3-induced co-stimulation will be tested. Markers associated with T cell co-stimulation will be assessed by analytical flow cytometry for their modulation by the primary peptide hits. The markers that will be analyzed are CD28, ICOS, CTLA-4, CDwl50 and CD40L (other markers may be added as deemed appropriate by the RMC). Peptides that demonstrate desirable characteristics will be used as bait in a genetic yeast two-hybrid screen to isolate their intracellular binding partner. These cDNAs will be validated by a number of assays to test whether they directly regulate T cell co-stimulation or not. Figure I summarizes the interrelationship of the various methods described above to map functional targets in T cell activation.

FIGURE 1

DIAGRAM

2.2 Secondary assays measuring T cell differentiation into Th1 and Th2 cells in T cell lines and primary human PBL T cells

Confirmed peptide hits from the primary functional screens will be subjected to secondary assays in T cell lines and primary peripheral blood and splenic T cells. In these assays, the effects of the hits on Th1/2 development will be tested. Markers associated with Th1/2 development will be assessed by analytical flow cytometry for their modulation by the primary peptide hits. The markers that will be analyzed are IL-12R-alpha and beta-2 chains, IFN-gamma-R-beta chain, ESTE-2, CD45RA, CD45RO and CD148 (other markers may be added as deemed appropriate by the RMC). Peptides that demonstrate desirable characteristics will be used as bait in a genetic yeast two-hybrid screen to isolate their intracellular binding partner. These cDNAs will be validated by a number of assays to test whether they directly regulate Th1/2 development or not. Figure 1 summarizes the interrelationship of the various methods described above to map functional targets in T cell activation.

EXPERIMENTAL DESIGN AND METHODS

PROJECT I.

IDENTIFICATION OF REGULATORY PROTEINS THAT AFFECT T CELL ACTIVATION.

RATIONALE:

T cells are pivotal in determining the type of immune response and its duration. Alterations in T cell activation and regulation are implicated in numerous diseases such as acute and chronic inflammation, autoimmunity and graft rejection. The screens in this approach will identify T cell activation-specific signaling molecules and assess their bias towards co-stimulation and/or Thl/2 development. This will permit specific intervention into T cell-mediated processes that contribute to or are the basis of disease.

1. PRIMARY SCREENS.

1.1 Primary peptide screen for inhibition of CD25 in T cells stimulated through CD3+/-CD28

Several T cell lines, including MOLT, Jurkat, Hut-102, Hut-78 and those to be determined by the Novartis - Rigel Joint Research Committee, will be tested for the presence of surface CD3. Those that express CD3 will be cultured with anti-CD3 to crosslink the TCR and test for the upregulation of CD25 and production of IL-2 (Appendix A). It is important that the kinetics and levels of expression of these markers overlap those observed in anti-CD3 stimulated primary human T cells.

PEPTIDE LIBRARY SCREENING AND PROTEIN TARGET IDENTIFICATION.

Cell lines selected as described above will be infected with one of 4 peptide libraries containing random 12 or 18 mer peptides on loop 3 or 4 of a BFP scaffold. Each of the peptide libraries will be packaged into infectious viral particles (for protocol, see Appendix E). Each library sequence will be upstream of a reporter gene to identify and/or select for infected cells and relative peptide expression (Appendix F). Likewise, for hit confirmation, each individual peptide sequence will be engineered into the same retroviral vectors upstream of a reporter gene.

We have developed several retroviral constructs to control all aspects of

peptide expression and localization. This gives us great flexibility when designing retroviral libraries within any cell line and with whatever characteristics are deemed necessary for intracellular peptide expression (see Appendix G). Constrained peptides have many valuable features compared to linear peptides, including enhanced resistance to proteolysis and a restricted conformation space that can result in a higher binding affinity for cognate binding proteins.

Each screen will start with production of the primary retrovirus peptide library. The primary library will be used to infect 10(8) to 10(9) T cells. After infection, the cells will be stimulated with anti-CD3 and, two days later, those cells containing a library member (positive for the fluorescent reporter) and inhibited for surface expression of CD25 will be enriched by FACS. This enriched population will be subjected to biological rescue to amplify and transfer the integrated peptide sequences to naive cells. The process will be repeated

until significant alteration in the expression of CD25 is observed by FACS. At this point, individual peptide sequences will be cloned and tested in the original screening assay for their ability to alter phenotype.

It will take approximately 4-6 rounds of enrichment to identify individual sequences capable of inhibiting TCR induction of CD25. For a discussion of the statistics associated with enrichment, see Appendix H. The most important factor that influences the number of enrichment rounds necessary to identify individual peptide hits is the ratio between real positive hits in the original library and heritable false positives. The frequency of real positive hits is dependent upon the qualitative ability of the over-expressed library member to alter the pathway of interest. Enrichment of real positive peptides becomes less efficient with false positive rates above 2%. For this reason, great effort is placed in developing robust cell lines.

To obtain phenotypic enrichment in the primary screens, the desired phenotype must be transferred from the enriched library-infected population to a naive population repetitively. Historically, we have used RT-PCR to rescue library members from the phenotypically desirable cells of one round, generate a new retroviral library and infect naive cells to enrich once again for the desired altered cell phenotype. Although RT-PCR works, uneven amplification will decrease overall amplification of real peptide hits from one round to another. Additional rounds of library enrichment can overcome this overall decrease of real hit amplification. However, to overcome the potential problems of RT-PCR and for more efficient transfer of phenotype from one round to the next, we are replacing RT-PCR amplification with a direct biological rescue (Appendix I). Biological rescue involves direct transfer of recombinant retroviral inserts from positively identified cell clones into naive cells for re-testing. By supplying retrovirus proteins GAG-POL-ENV to library-enriched cells, integrated proviral transcripts encoding putative peptide hits are selectively re-packaged and secreted as new virions capable of infecting new cells. Positive cells can be converted to retroviral producers by superinfection of GAG-POL-ENV genes or alternatively, tetracycline-inducible packaging functions can be pre-engineered into target cell lines. By either strategy, peptides from enriched cells can be selectively transferred to new cells and re-tested for phenotypic effects, eliminating the time-intensive and potentially biased intermediary molecular cloning steps. Proof of principle demonstrating the feasibility of this approach is shown in Appendix J.

1.2 Functional screening for inhibitors of TCR-induced transcription of the IL-2 promoter in cell lines carrying the IL-2 promoter upstream of a reporter fused to death genes

An alternative to the flow-based screens outlined above is to generate cell lines that survive when promoters critical to T cell activation are inhibited. This is a very stringent assay with very low background. This is accomplished by infecting CD3-inducible T cell lines with the following construct: A retroviral vector containing a TCR-responsive fragment of the IL-2 promoter in the reverse orientation followed by a splice site, a reporter gene such as GFP, an IRES and finally a fusion of two death genes, TK and CD (Appendix B). The determination of the appropriate death genes to use will be dependent on which is most robust in the particular T cell line chosen. Briefly, cells will be infected with the reporter/death gene construct and induced with anti-CD3. Cells expressing higher levels of GFP will then be enriched by FACS. The anti-CD3 will be removed and the cells will be enriched for absent or decreased reporter fluorescence. Alternatively, pools of infected cells are divided and grown in parallel so that one set can be induced and tested for GFP/death

gene induction without having to subject its sibling to TCR engagement. This will control for any lasting effect TCR engagement may have on the GYP reporter and the fused death genes.

The method will be as follows: The survival cell lines from above are infected with the desired library (Appendix E). Leaky cells (constitutive expression of the IL-2 promoter) are not a concern since the addition of the second signal is required to kill cells. The second signal will be withheld until the library has had time to express allowing all possible promoter inhibitors to manifest. Two days after library infection, the cells are induced with anti-CD3 in the presence of the appropriate death signal (ganciclovir for TK and 5-FC for CD). Cells carrying peptides that inhibit induction of the engineered IL-2 promoter fragment will not produce the death genes and will survive. After the survivors grow out (approximately 1 week), they will again be subjected to anti-CD3 and the death signals. The genes encoding the peptides responsible for the survivors will be transferred to naive cells by biological rescue as previously described (section 1.1). The identification of individual inhibitory peptides should occur in only 3-4 rounds since the false positive background for survival screens is lower than for FACS-based screening. Once enrichment is achieved and individual sequences are independently shown to inhibit IL-2 promoter activation, these sequences will be introduced into a standard set of secondary and orthogonal assays as described below in section 2. As well, the proteins they interact with will be identified as discussed in section 3 below.

2 SECONDARY ASSAYS TO ASSESS PHYSIOLOGIC CHARACTERISTICS AND SPECIFICITY OF PRIMARY FUNCTIONAL PEPTIDE HITS.

2.1 Secondary assays measuring expression of cell surface T cell co-stimulatory molecules in T cell lines and primary human PBL T cells stimulated through CD3 +/-CD28

After library enrichment, individual sequences shown to modulate CD25 expression or IL-2 promoter activation will be introduced into a standard set of secondary assays. The overall aim of these assays is to test the specificity and physiologic characteristics of the functional peptide hits. This will be a critical step in determining priority of hits for more intensive investigation. Many of these assays will be performed in T cell lines and primary peripheral blood or splenic T cells. The ability of the hits to alter anti-CD3 induced expression of co-stimulatory molecules will be measured. These include but are not limited to CD28, ICOS, CTLA-4 CDwl50 and CD40L. Functionally validated peptide hits will then be used as bait to isolate their interacting protein targets by genetic (yeast two-hybrid) screening technologies (see section 3 for yeast two-hybrid details). These new interacting partners can be cycled into the functional assays to assess their specific role in T cell signaling. In this manner, activation pathways that mediate multiple functions in T cells can be deconvoluted in a step-wise manner.

2.2 Secondary assays measuring T cell differentiation into Th1 and Th2 cells in T cell lines and primary human PBL T cells

Just as described above in section 2.1, peptide hits from the primary screens will be tested for their ability to influence Thl/2 development. CD3 activation combined with the presence of the appropriate cytokines will bias T cells towards Thl or Th2 development. Cell surface markers such as IL-12R (alpha) and (beta)2 chains, IFN-(gamma)R (beta) chain, ESTE-2, CD45RA, CD45RO and CD148 have been shown to be associated Thl/2 development. The peptide hits will be assessed for their ability to modulate these markers. They will also be tested for their

ability to alter the secretion of cytokines associated with Thl (IFN-(gamma)) and Th2 responses (IL-4).

Functionally validated peptide hits will then be used as bait to isolate their interacting protein targets by genetic (yeast two-hybrid) screening technologies (see section 3 for yeast two-hybrid details). These new interacting partners can be cycled into the functional assays to assess their specific role in T cell signaling. In this manner, activation pathways that mediate multiple functions in T cells can be deconvoluted in a step-wise manner.

PROJECT I - PATHWAY MAPPING.

FUNCTIONAL MAPPING OF NOVEL T CELL SIGNALING PROTEINS.

3.1 Yeast two-hybrid screening, to identify and map proteins that interact with functional peptide hits.

Peptides that modulate lymphocyte activation do so by binding to intracellular proteins that are members of signal transduction pathways which ultimately lead to diverse phenotypic endpoints in T cells. Identification of functional peptide-target protein pairs in these pathways will enable subsequent screening for low molecular weight compounds that alter T cell function.

Priority peptide hits from the library screens that alter lymphocyte activation will be subjected to yeast two-hybrid screening to identify their intracellular binding partners. The libraries to be screened are described in

section 1 above. The screening protocol for identification of interacting proteins is summarized in Appendix D. Briefly, sequences encoding the target peptides will be cloned into pAS2-1K to fuse to the C-terminal of GAL4 DNA binding domain. The oligos can also be cloned into pAS2N to fuse to the N-terminal of GAL4 DNA binding domain. Both bait plasmids can be used for subsequent screenings. The bait plasmids will be transformed into the Y190 yeast strain. This yeast strain has the highest sensitivity for yeast two-hybrid screening. Optimal 3AT concentration needed to suppress any HIS background expression will be determined on SD-WH+3AT plates. The cDNA libraries will be fused with the GAL4 activation domain and transformed into the yeast already containing the bait plasmid. At least 20 million transformants from each library will be screened on SD-LWH+3AT plates. HIS+ and LacZ+ clones will be grown up in SD-L liquid medium to retrieve plasmid and for retransformation into Y190 to verify the binding specificity.

Isolated proteins that are determined to interact with the functional sequence baits will be tested for their ability to affect T cell activation in the previously discussed secondary assays. The various ways to determine function in the secondary assays is by simple overexpression of the putative target protein and any potential dominant-negative domains, and random mutagenesis to destroy functioning domains (Appendix K).

INITIAL STEPS FOR TARGET IDENTIFICATION/VALIDATION (SEE FLOWCHART IN APPENDIX L).

It is important to recognize that once a target protein/peptide pair has been identified, the relationship between that target protein and the pathway of interest for that particular cell type is defined by virtue of the functional screen that produced it. False positives arise only if the hit binds to additional proteins not related to the functional pathway of interest. The

binding peptide minimizes this possibility as it binds to only a portion of the cDNA in a manner that regulates the pathway of interest. Below is a protocol to discriminate false positives from pathway-specific protein/peptide target pairs.

Once the desired change in the phenotype of the library-infected cells is achieved, the cDNAs/peptides responsible will be sequenced. Individual sequences derived from the libraries, and subsequently two-hybrid approaches will be tested for their ability to alter T or B cell activation as described earlier. Targets are defined as functional cDNAs whose binding peptide can alter its influence on lymphocyte activation in a desired way.

The protein/peptide pairs can be subjected to numerous secondary assays to confirm their role and specificity in lymphocyte activation/regulation. The type of protein/peptide pairs identified will dictate the exact assays performed. These assays include over-expression in lymphocytes of the target protein, their individual functional domains, dominant negative mutants (large-scale mutagenesis of specific cDNAs to generate libraries of "mutant targets," see Appendix L) and anti-sense mRNA of the target protein sequence. The readouts will include changes in the expression of activation-upregulated surface proteins, cytokine production and proliferation as described in Section 1 and 2. In addition, the ability to revert the phenotype of activated lymphocytes by over-expressing the target protein in cells expressing the inhibitory binding peptide will be tested. These assays will assist the Joint Novartis-Rigel Research Committee in their determination of targets to be introduced into Novartis small molecule compound screens. Below is a brief description of the rationale and approach for each of the assays described above.

Over-expression of the target protein or individual functional domains may modulate lymphocyte activation, thereby implicating the specific protein in one of the activation-coupled intracellular regulatory pathways. This can be accomplished very simply with Rigel's retroviral vector system. By using reporter genes downstream of the cDNA-encoding the target protein or domain, we can track infected cells and determine the relative production of the target protein/domain. This will allow us to titrate its biological effect as a means to confirm the target protein's role in lymphocyte activation. If overexpression of the protein target influences T cell activation, mutant libraries of the protein can then be screened for loss-of-function as described below.

Target proteins will be randomly mutated (see Appendix L) and screened in the FACS assays described in Section 1 for mutant proteins that alter lymphocyte activation. Two variations of this approach allow us to narrow our screen of mutant target proteins. One variation is to perform mutagenesis on the target cDNA and then subject the mutagenized target to a two-hybrid screen with the cognate peptide as bait to identify mutants that no longer bind the peptide. These mutant proteins can be tested for loss-of-function in mammalian cells. Alternatively, the peptide can be chemically crosslinked to the target protein to identify the region bound by the peptide using mass spectrometry. Subsequently, the peptide-binding region of the target protein is randomly mutated and the clones screened for their ability to inhibit lymphocyte activation. The advantage of this variation is that the regulatory domain of the target protein is identified.

A third approach to confirm the role of the target protein in lymphocyte activation is to overcome peptide inhibition by overexpressing the target protein. The screening cell lines are infected with the peptide and its target protein where the target protein under the control

of an inducible promoter such as tetracycline or metallothionein. When the target protein is induced, its ability to outcompete inhibition by the peptide can be tested.

Some or all of the above methods can be employed to confirm that a protein/peptide pair, identified in the initial screen is functionally relevant. Because of our retroviral technology virtually any strategy of intracellular expression can be approached to verify protein/peptide target pairs in living cells. It will be the task of the Joint Novartis-Rigel Research Committee to determine which assays are necessary to sufficiently define a functional protein/peptide pair for the next phase of development, specifically small molecular weight compound screening.

HEADCOUNT

To run optimally, the T cell project (Project I) and the B cell project (Project II) will each take 12 full-time Rigel FTEs. Listed here are the scientists who would begin working on the T cell project:

DAVID FERRICK: Dr. Ferrick is the project director and is the primary supervisor responsible for ensuring the project hits milestones and objectives in a timely mariner. In addition, he is the head of Molecular and Cell Biology and will supervise all aspects of the various constructs, library generation, library enrichment steps, target validation, and target analysis. Also, he is responsible for the supervision and data analysis resulting from the HTS FACS analysis/sorting.

CHARLENE LIAO: Dr. Liao is the project leader and will coordinate all communication between Rigel and Novartis. She will be responsible for the development of all primary and secondary assays for the screens. She will generate the IL-2 promoter survival cell lines and oversee their screening. She is responsible for analyzing the function of individual peptide and protein hits in cell lines and primary cells.

PEIWEN YU: Dr. Yu is a Scientist who is investigating functional T cell targets and two-hybrid hits. She is involved in developing many of the functional assays related to T cell function.

TBH: A Scientist is required to be in charge of retroviral library design and production. He will be responsible for the generation of all peptide libraries with their scaffold and localization sequences. He will perform library rescue and the subsequent subcloning of the individual peptide hits. He will also shuttle hits from the yeast two-hybrid screen to mammalian vectors for post two-hybrid functional analysis.

S. SWIFT: S. Swift is the Senior Research Associate in charge of retroviral production and tissue culture. She is responsible for conducting the library screens, which involves the generation of the infectious library for each round of enrichment screening and all aspects of tissue culture associated with the screening effort. She is also coordinating and performing biological rescue to transfer enriched peptide clones from one round to the next, as well as RT-PCR isolation of individual peptide sequences.

G. MINTIER: G. Mintier is the Research Associate responsible for retroviral vector design and testing. He will generate the retroviral constructs to be used in all the screens. He will be responsible for performing the peptide screens and conducting the rescue of the hits from those screens. He will be involved in the screening for proteins that bind the peptide hits.

H. KHOSHNEVISAN: H. Khoshnevisan is a cell biology Research Associate responsible for all the tissue culture work for the project. She maintains all the different lymphocyte cell lines, the Phoenix packaging cell line, and the sorted cell populations.

M. AUJAY: M. Aujay is the Research Assistant in charge of the sequencing core. She will be responsible for all DNA sequencing on this project. This includes sequencing of all rescued libraries to check for enrichment and contamination, all verified peptide hits, and two-hybrid hits. She is also responsible for managing the sequence database and all related

DNA bioinformatics of the project. She will coordinate the data entry into the appropriate databases.

P. FALLON: P. Fallon is the Senior Research Associate in charge of the high-speed flow cytometry core. He is responsible for setting-up and implementing all the FACS-based assays. He will be responsible for adapting all assays for FACS-based sorting. He will perform these assays and sort the library hits. He will also supervise the FACS-associated bioinformatics for all the screens.

B. HUANG: B. Huang is an Intracellular Pathway Mapping Manager in charge of two-hybrid screening. She is responsible for setting up and carrying out all the two-hybrid assays, analyzing and isolating full-length clones, and generating the cDNA libraries.

D. HATRAN: D. Hatran is a molecular biology Research Associate in the target identification group. He is responsible for all the support work on the one- and two-hybrid analyses, including media prep, plate pouring, minipreps, colony picking, gel analysis, and subcloning.

C. LAU: C. Lau is a Research Associate responsible for all the subcloning of hits into expression vectors and execution of secondary assays to verify function in primary cells. She will also perform various labor-intensive tasks associated with the screening effort such as peptide rescue, library sequencing and tissue culture.

12.

APPENDIX A

[DIAGRAM]

13.

APPENDIX B

[DIAGRAM]

14.

APPENDIX C

[DIAGRAM]

15.

APPENDIX D(1)

[DIAGRAM]

16.

APPENDIX D (2)

[DIAGRAM]

17.

APPENDIX E

PROTOCOL FOR TRANSFECTION OF PHOENIX CELLS AND INFECTION OF NONADHERENT TARGET CELLS

[DIAGRAM]

DAY 1:

Seed Phoenix cells (Es or As) in 10cm plates at 5 x 10(6) cells in 6 ml (DMEM + 10% FBS + Pen/Strep) per plate the day before transfection.

DAY 2:

Allow all reagents to reach room temperature 30 min. before starting. Add 50 mM chloroquine at 8 microl/plate (50 microM final) before preparing the transfection solution.

Mix CaPO4 reagents in 15ml polypropylene tube:

per plate: 10 microg. DNA
122 microliter 2M CaCl(2)
876 microliter H20
1.0ml 2X HBS

Add 2X HBS and depress the expulsion button completely to bubble air through the mix for 10 secs. Immediately add mixture gently dropwise to plate.

Incubate 3-8 hours.

Remove medium and replace with 6.0 ml DMEM-medium.

DAY 3:

Change medium again to 6.0 mls of medium optimal for the cells to be infected. Move to 32(degree) C either in the morning or afternoon depending on the Phoenix cell confluency and whether you will infect at 48 or 72 hrs after transfection.

DAY 4 OR 5:

Collect virus supernatant from transfected plates (6.0 ml) into 50 ml tubes and add protamine sulfate to a final concentration of 5 microg./ml.

Pass through a 0.45 micrometer filter.

Count target cells and distribute 10(7) cells per 10 cm plate transfected to 50 ml tubes and pellet 5 min.

Resuspend each pellet of target cells in virus supernatant and transfer to a 6 well plate at 1.0-1.2 ml per well.

Seal plate with parafilm and centrifuge at RT for 30-90 min. at 2500 RPM.

Remove parafilm and incubate plate over night at 37(degree)C.

DAY 5:

Collect and pellet each well of target cells. Resuspend in 3 ml medium and transfer back to the same 6well plate.

Infection can be repeated by refeeding the Phoenix cells with 6ml fresh medium and reinfecting the same cells again up to 3 times to increase % of cells infected (for instance at 48, 56, and 72 hours)

DAY 7 OR DAY 8:

At 48 to 72 hrs. post infection, target cells are ready to analyze for expression.

APPENDIX F

[DIAGRAM]

APPENDIX G

[DIAGRAM]

APPENDIX H

[DIAGRAM]

APPENDIX J

[DIAGRAM]

APPENDIX K

[DIAGRAM]

24.

APPENDIX L (1)

[DIAGRAM]

25.

APPENDIX L(2)

[DIAGRAM]

26.

Rigel-Novartis Collaboration

[DIAGRAM]

27.

EXHIBIT A-2

B-CELL PROGRAM OF RESEARCH

Provisional Draft

NOVEL REGULATORY PATHWAYS IN T AND B LYMPHOCYTES

NOVARTIS PROJECT OUTLINE

PROJECT II: IDENTIFICATION OF REGULATORY PROTEINS THAT AFFECT BCR-INDUCED IG PRODUCTION

INTRODUCTION

Activation of specific signaling pathways in lymphocytes determines the quality, magnitude and duration of immune responses. In transplantation, acute and chronic inflammatory diseases, and autoimmunity, it is these pathways that are responsible for the induction, maintenance and exacerbation of disease lymphocyte responses. Of the many activation pathways that have been elucidated, most are ubiquitous and not unique to a particular cell lineage. The goal of this proposal is to identify and validate novel (signaling) molecules specific for B cell activation and effector function as potential pharmacological targets for B cell inhibition. From these molecules, B cell-specific targets will be identified that are effective in modulating immune-mediated processes. A combination of high throughput functional and yeast two-hybrid genetic screens will be employed to isolate and map novel (signaling) molecules essential for lymphocyte activation. Engagement of the B cell receptor (BCR) together with additional activation principals stimulates humoral immunity characterized by immunoglobulin production and antigen presentation by B cells. Summarized below, in Table 1, are four strategies for identifying and validating novel B cell intracellular signaling molecules. Each approach, its readout, and the libraries to be used are detailed in the remaining sections of the proposal. Two of these approaches (to be chosen by the Joint Novartis-Rigel Research Management Committee) will be pursued initially.

PREFINAL DRAFT -- ELEMENTS YET TO BE FINALIZED

1.

TABLE 1. SUMMARY OF SCREENS TO IDENTIFY INTRACELLULAR REGULATORS OF LYMPHOCYTE ACTIVATION AND/OR EFFECTOR FUNCTION.

<TABLE>
<CAPTION>
- ----------
PROJECT II
IDENTIFICATION OF REGULATORY
PROTEINS THAT AFFECT BCR-
INDUCED IG PRODUCTION

APPROACH	READOUT	LIBRARY
1. PRIMARY SCREENS		
1.1 SCREEN 1: Primary peptide screen looking for signaling molecules involved in BCR activation as measured by inhibition of B cell activation marker up-regulation	Enrichment by FACS for decreased expression of multiple B cell activation markers	Puromycin and BFP loop3 scaffold peptide libraries (12 mer and 18 mer)
1.2 SCREEN 2: Primary peptide screen for inhibitors of IgH chain promoter activity in a B cell line stimulated through the BCR	Isolation of survivors and enrichment by FACS for absent or decreased reporter activity	Potential additional libraries (constrained 18mer, Beta-lactamase based, DHFR-based) to be determined by the RMC
1.3 SCREEN 3: Primary peptide screen for inhibitors of secretory Ig expression as measured by TK/GFP transgene in a mature B cell line	Isolation of survivors and enrichment by FACS for absent or decreased reporter activity	
1.4 BACKUP SCREEN: Primary peptide screen for signaling molecules involved in BCR activation as measured by apoptosis	Isolation of survivors	
2. SECONDARY ASSAYS		
2.1 BCR-induced IG secretion in primary B cells and cell lines	Secretion of Ig as measured by ELISA. Production of Ig secretory transcript as measured by PCR	
2.2 A collection of BCR-induced proliferative responses in primary B cells and cell lines; Specificity of hits in alternative cell types	(3)H-thymidine incorporation, FACS for NFAT reporter gene assay and cell surface marker up-regulation, ELISA for Ig switching; T cell and macrophage activation marker expression	

</TABLE>

EXPERIMENTAL DESIGN AND METHODS

IDENTIFICATION OF REGULATORY PROTEINS THAT AFFECT B CELL ACTIVATION

1. Primary Screens

During xeno-transplantation, the initial hyperacute rejection is predominantly mediated by complement and secretory Ig. Inhibition of secretory Ig production may result in suppression of the rejection. Therefore, the primary goal of our screen is to identify protein targets that are involved in the pathways that lead to the production and secretion of Ig. Three different primary screening strategies and a backup screen are proposed which have distinctive advantages and disadvantages (Appendix A). The knowledge obtained from these screens provides a comprehensive perspective on this complex and intractable area in a manner not possible with any single approach.

1.1 Screen 1: Primary peptide screen looking for signaling molecules involved in BCR activation as measured by inhibition of B cell activation marker up-regulation.

RATIONALE:

The first approach involves screening peptides that directly inhibit the up-regulation of multiple cell surface markers related to B cell signaling that are upstream or connected to the Ig secretion pathway. This approach is based on multiple marker sorting and can lead to the discovery of proliferative signaling molecules in the BCR pathway:

CELL LINES, CONSTRUCTS, AND ACTIVATION MARKERS:

Four activation markers will initially be evaluated for their up-regulation upon anti-Ig activation (e.g. CD69, IL-5R, surface Ig, MHC Class II, and Ca2+ mobilization). Expression of the activation markers will be optimized to ensure the lowest background, a critical factor in our inhibitory peptide screens. It will also be important to ensure that the signaling event triggered by FACS sorting is reversible so that multiple rounds of screening are possible.

A panel of Ig+ mature B cell lines will be tested for their ability to upregulate several key activation markers in response to BCR engagement. Those with the greatest dynamic range of primary B cell activation will be employed in the primary screens. The selected cell lines will then be infected with the Tet-off transactivator tTA and TRE-LYT2 producing viruses (Appendix B). The integration of the tTA plasmid will be selected by hygromycin; background of TRE promoter and the expression of tTA will be selected according to LYT2 expression. High level of induction and low background of tTA activity will determine the feasibility of the Tet-regulated system in the appropriate cell line.

PEPTIDE LIBRARY SCREENING AND PROTEIN TARGET IDENTIFICATION:

Cell lines selected as described above will be infected with one of Rigel's peptide libraries. We have developed several retroviral constructs to control all aspects of peptide expression and localization. This gives us great flexibility when designing retroviral libraries within any cell line and with whatever characteristics are deemed necessary for intracellular peptide expression (Appendix C). Constrained peptides have many valuable features compared to linear peptides, including enhanced resistance to proteolysis and a restricted

conformation space that can result in a higher binding affinity for cognate binding proteins. In order to screen for as great a range of targets as possible, three different libraries driven by the Tet-off, TRE promoter will be used initially: two constrained libraries (a 12 mer and an 18 mer library inserted at loop 3 of a BFP scaffold) and a linear library fused directly to a puromycin resistance gene (18 mer). Dependent upon the results of the screens using these libraries, the RMC may determine other library scaffolds should also be utilized (e.g. constrained 18 mer, (beta)-1actamase based, enzyme based).

These primary libraries will be used to infect 10(8) to 10(9) B cells (Appendix D) and the cells will be grown without Dox to allow peptide expression (Appendix E). The cells will be stimulated with anti-Ig and selected for loss of up-regulation of the cell surface markers. This population of cells contains either inhibitory peptides or somatic mutations. To remove somatic mutations, the cells will be grown out in the presence of Dox (peptide expression turned off), followed by sorting for up-regulation of surface markers after stimulation with anti-Ig. The GFP positive cells can then be funneled into multiple rounds of selection, carried out by turning the peptides on and off until a definitive peptide-dependent phenotype is obtained. After the final round of enrichment, the GFP positive cells (peptide off) will be sorted into individual wells of duplicate 96-well plates and treated +/- Dox. Peptide sequences from those cells exhibiting the appropriate phenotype will then be isolated and transferred to a naive population of cells. Their phenotype will be verified as being peptide-dependent on an individual sequence basis.

This screen may have significantly higher background than the other screens and, therefore, may take longer to identify hits. However, there is an advantage in that inhibitors with complex phenotype can be isolated using this approach.

1.2 Screen 2: Primary peptide screen for inhibitors of IgH promoter activity in a mature B cell line stimulated through the BCR.

RATIONALE:

The effect of BCR activation on IgH production is two fold: the IgH promoter activity is enhanced and there is an immediate increased production of the secretory form of Ig. Inhibitors that block Ig(mu) promoter activity inhibit an upstream event of all Ig production, which may or may not inhibit the translational control of the pre-existing mRNA of Ig. However, in either case, therapeutic targets identified which block Ig production will be relevant for hyperacute rejection (minutes-hours). In addition, since antibody production is considered to be important during chronic rejection (months-years), the targets found in this screen may also be particularly useful in later stages of rejection.

CONSTRUCTS AND CELL LINES:

In order to carry out the screen, an Ig+ mature B cell line that has robustly enhanced activity of IgH promoter upon BCE signaling will be obtained. A construct with a GFP/TK fusion driven by an IgH promoter will be used

(Appendix F). Regions of the IgH promoter that confer the lowest background and the highest inducibility will be determined in the selected cell line. The Tet-off transactivator will then be integrated into the chosen cell line as described in Screen 1 (Section 1.1).

PEPTIDE LIBRARY SCREENING AND PROTEIN TARGET IDENTIFICATION:

Cell lines selected as described above will be infected with one of Rigel's peptide libraries as described in screen 1.

These primary libraries will be used to infect 10(8) to 10(9) B cells. The cells will be grown out in media without Dox, which allows for peptide library expression (Appendix G). Cells will be stimulated with anti-Ig antibodies, and selected in ganciclovir. Cells containing the TK reporter will be killed by the ganciclovir unless a peptide inhibitor is present which inhibits the gene's expression (Appendix H). The peptide-containing survivors will be enriched by FACS for GFP negative cells (containing an inhibitor of the GFP reporter). This will remove residual GFP-expressing cells that were not eliminated by the ganciclovir. The cells that do not fluoresce will contain either peptides or somatic mutations that inhibit alternative splicing or protein synthesis. To remove the background caused by somatic mutations, the cells will be grown in the presence of Dox (to turn off peptides) and (alpha) Ig allowing GFP/TK to express. The GFP positive cells will be sorted into individual wells of a 96-well plate. Triplicate plates will be grown in different combinations of Dox and ganciclovir to confirm that the phenotypic change is due to the peptide. The peptides will then be isolated from those cells and transferred to a naive population of cells where their phenotypes will be verified as being peptide-dependent on an individual sequence basis.

1.3 Screen 3: Primary peptide screen for inhibitors of secretory Ig expression as measured by TK/GFP transgene in a mature B cell line.

RATIONALE:

This strategy searches for inhibitors of Ig secretion and is the most direct measure of the goal as defined in this proposal. This approach will directly target the splicing step and translation of the IgH chain that is responsible for generating the secretory form of Ig.

Increased promoter activity after BCR ligation and/or increased stability of Ig(mu) mRNA in B cells are thought to be critical for the enhanced level of RNA message. The understanding of the contributions of these two phenomena during B cell development and immune responses has been elusive. However, this approach should allow for the discovery of drug targets in either case.

CELL LINES AND CONSTRUCT:

Ig+ mature B cell lines will be tested for their ability to produce secretory Ig. The most inducible cell line will be infected with a retroviral construct containing a TK/GFP fusion gene inserted after (mu)4, the secretory segment (S) and the puromycin resistance gene following the cytoplasmic exon (Appendix I). Cells will be selected in puromycin to obtain a population that contains stably integrated transgenes. Upon anti-Ig stimulation, GFP and TK activity will reflect the expression of the secretory forms of Ig. Before screening, the physiological nature of the BCR-induced splicing event in both the endogenous and the transgene will be confirmed using PCR analysis. The tTA expressing cell line will be generated as described in Screen 1.

PEPTIDE LIBRARY SCREENING AND PROTEIN TARGET IDENTIFICATION:

The screening protocol will be identical to that described in Screen 2 (Appendix G).

1.4 Back-up Screen: Primary peptide screen for inhibition of BCR signaling measured by apoptosis in a mature or immature B cell line.

RATIONALE:

This screen is based on the assumption of cross-functionality between proliferative and apoptotic pathway members and is presented as a back-up strategy.

The outcome of BCR activation can be either apoptotic or proliferative, depending on the concentration and binding affinity of the antigen, the developmental stage of the B cells, and the coatimuli provided by T cells. Current understanding indicates that great similarities exist between the death and survival pathways. Based on this expectation of cross-functionality between pathways, an apoptotic approach was used to identify several important molecules in the TCR proliferative signaling pathway, including Lck, SLP-76 and LAT.

Similarly, the apoptotic screening strategy described here will allow a rapid discovery of BCR signaling molecules that are involved Ig production and/or secretion in a system with low background. Specific secondary assays will then be used to confirm the cross functionality of the molecules in BCR-induced Ig secretion and B cell proliferation.

CELL LINE:

A mature or immature B cell line will be identified by the RMC that is efficiently induced to apoptose upon hypercross-linking or cross-linking with different anti-Ig antibodies.

PEPTIDE LIBRARY SCREENING AND PROTEIN TARGET IDENTIFICATION:

The peptide scaffold for the primary libraries described in Screen 1 - 3 will be used to infect 10(8) to 10(9) B cells. Unlike the earlier screens; however, these libraries will not be under Tet control. The cells will be infected, allowed to express the peptide library, and stimulated with (alpha)-Ig (Appendix J). The survivors, containing inhibitory peptides or somatic mutations, will then be subjected to biorescue which transfers the peptide sequences to a naive population of cells (method of transfer described below). Multiple rounds of selection will be performed until the survival rate is sufficiently greater than that of the control. Somatic mutants that survive the initial selection will not be transferred when the peptides are reintroduced into a naive population.

To obtain phenotypic enrichment in the primary screens, the desired phenotype must be transferred from the enriched library-infected population to a naive population repeatedly. Historically, we have used RT-PCR to rescue library members from the phenotypically desirable cells of one round, then generated a new retroviral library and infected naive cells to enrich once again for the desired phenotype. Although this approach works, uneven amplification decreases overall amplification of real peptide hits from one round to another. Additional rounds of library enrichment can overcome this overall decrease of real hit amplification. However, to avoid the potential problems of RT-PCR and for more efficient transfer of phenotype from one round to the next, we are replacing RT-PCR amplification with a direct biological rescue (Appendix K). Biological rescue involves direct transfer of recombinant retroviral inserts from positively identified cell clones into naive cells for re-testing. By supplying retrovirus proteins gag-pol-env to library-enriched cells, integrated proviral transcripts encoding putative peptide hits are selectively re-packaged and secreted as

new virions capable of infecting new cells. Positive cells can be converted to retroviral producers by superinfection of gag-pol-env genes or alternatively, tetracycline-inducible packaging functions can be pre-engineered into target cell lines. By either strategy, peptides from enriched cells can be selectively transferred to new cells and re-tested for phenotypic effects, eliminating the time-intensive and potentially biased intermediary molecular cloning steps. Proof of principle demonstrating the feasibility of this approach is shown in Appendix L.

It will take approximately 3-4 rounds of enrichment to identify individual sequences capable of altering phenotype above background. For a discussion of the statistics associated with enrichment, see Appendix M. The most important factor that influences the number of enrichment rounds necessary to identify individual peptide hits is the ratio between real positive hits in the original library and heritable false positives. The frequency of real positive hits is dependent upon the qualitative ability of the over-expressed library member to alter the pathway of interest. Enrichment of real positive peptides becomes less efficient with false positive rates above 2%. For this reason, great effort is placed in developing robust cell lines.

2. SECONDARY ASSAYS TO ASSESS PHYSIOLOGIC CHARACTERISTICS AND SPECIFICITY OF PRIMARY FUNCTIONAL PEPTIDE HITS.

2.1 Secondary assays measuring Ig secretion in B cell lines and primary human PBL B cells stimulated through the BCR.

After library enrichment, individual sequences shown to modulate BCR signaling and/or Ig secretion will be introduced into a standard set of secondary assays. The overall aim of these assays is to test the specificity and physiologic characteristics of the functional peptide hits. This will be a critical step in prioritizing hits for more intensive investigation. These assays will be performed in B cell lines and primary peripheral blood or splenic B cells. Of primary importance will be the ability of the hits to alter anti-Ig induced Ig secretion either by directly inhibiting secretion or indirectly by blocking activation events leading to Ig secretion. Inhibition of Ig by the hits will be measured by ELISA in both cell lines and primary human B cells. For further confirmation and to assess the mechanism of inhibition, the hits will be tested for their ability to block the alternative splicing of the secretory Ig transcript measured by PCR analysis. The block of the Ig secretory pathway will

also be measured by western analysis for the cytoplasmic retention of the smaller form of the Ig heavy chain.

Functionally validated peptide hits will then be used as bait to isolate their interacting protein targets by genetic (yeast two-hybrid) screening technologies (see section 3 for yeast two-hybrid details). These new interacting partners can be cycled into the functional assays to assess their specific role in Ig secretion. In this manner, activation pathways that mediate multiple functions in Ig secretion can be deconvoluted in a step-wise manner.

2.2 Additional assays to further characterize the specificity of hits that block Ig secretion.

In addition to secondary assays directly targeting Ig secretion, a combination of generic assays for BCR proliferative responses will also be used to clarify the role or mechanism of the primary hits that block Ig secretion. Such assays (to be determined by RMC) may include calcium influx, 3H-thymidine incorporation, NFAT reporter gene assay,

cell surface marker up-regulation markers (such as IL-1R, IL-2R, IL-6R, CD10, CD23, and CD25), and Ig switching. In addition, the specificity of the hits will be assessed based upon their ability to inhibit TCR-mediated T cell activation, as well as LPS-induced macrophage activation.

Peptide hits validated in these activation, proliferation, and specificity assays will be cycled into yeast two-hybrid screens as described in section 2.1 and section 3.1.

PATHWAY MAPPING.

FUNCTIONAL MAPPING OF NOVEL B CELL SIGNALING PROTEINS.

3.1 Yeast two-hybrid screening to identify and map proteins that interact with functional peptide hits.

Peptides that modulate lymphocyte activation do so by binding to intracellular proteins that are members of signal transduction pathways which ultimately lead to diverse phenotypic endpoints in B cells. Identification of functional peptide-target protein pairs in these pathways will enable subsequent screening for low molecular weight compounds that alter T and B cell function.

Priority peptide hits from the library screens that alter BCR signaling will be subjected to yeast two-hybrid screening to identify their intracellular binding partners (Appendix N). The libraries to be screened will be derived from various populations of B cells. The screening protocol for identification of interacting proteins is summarized in Appendix O. Briefly, sequences encoding the target peptides will be cloned into pAS2-1K to fuse to the C-terminal of GAL4 DNA binding domain. The sequences can also be cloned into pAS2N to fuse to the N-terminal of GAL4 DNA binding domain. Both bait plasmids can be used for subsequent screenings. The bait plasmids will be transformed into the Y190 yeast strain. This yeast strain has the highest sensitivity for yeast two-hybrid screening. Optimal 3AT concentration needed to suppress any HiS background expression will be determined on SD-WH+3AT plates. The cDNA libraries will be fused with the GAL4 activation domain and transformed into the yeast already containing the bait plasmid. At least 20 million transformants from each library will be screened on SD-LWH+3AT plates. HIS+ and LacZ+ clones will be grown up in SD-L liquid medium to retrieve plasmid and for retransformation into Y190 to verify the binding specificity.

Isolated proteins that are determined to interact with the functional sequence baits will be tested for their ability to affect BCR signaling in the previously discussed secondary assays. The various ways to determine function in the secondary assays is by simple overexpression of the putative target protein and any potential dominant-negative domains, and random mutagenesis to destroy functioning domains (Appendix P).

INITIAL STEPS FOR TARGET IDENTIFICATION/VALIDATION (SEE FLOWCHART IN APPENDIX Q1 AND Q2).

It is important to recognize that once a target protein/peptide pair has been identified, the relationship between that target protein and the pathway of interest for that particular cell type is defined by virtue of the functional screen that produced it. False positives arise only if the hit binds to additional proteins not related to the functional pathway of interest. The

binding peptide minimizes this possibility as it binds to only a portion of the cDNA in a manner that regulates the pathway of interest. Below is a protocol to discriminate false positives from pathway-specific protein/peptide target pairs.

Once the desired change in the phenotype of the library-infected cells is achieved, the cDNAs/peptides responsible will be sequenced. Individual sequences derived from the libraries, and subsequently two-hybrid approaches will be tested for their ability to alter B cell activation as described earlier in Sections 1 and 2. Initial targets are defined as functional cDNAs whose binding peptide can alter its influence on lymphocyte activation in a desired way.

The protein/peptide pairs can be subjected to numerous secondary assays to confirm their role and specificity in lymphocyte activation/regulation. The type of protein/peptide pairs identified will dictate the exact assays performed. These assays include over-expression in lymphocytes of the target protein, their individual functional domains, dominant negative mutants (large-scale mutagenesis of specific cDNAs to generate libraries of "mutant targets," see Appendix P) and anti-sense mRNA of the target protein sequence. The readouts will include changes in the expression of activation-up-regulated surface proteins, antibody production, cytokine production and proliferation as described in Section 1 and 2. In addition, the ability to revert the phenotype of activated lymphocytes by over-expressing the target protein in cells expressing the inhibitory binding peptide will be tested. These assays will assist the RMC in their determination of targets to be introduced into Novartis small molecule compound screens. Below is a brief description of the rationale and approach for each of the assays described above.

Over-expression of the full-length target protein or individual functional domains may modulate B cell activation, thereby implicating the specific protein in one of the activation-coupled intracellular regulatory pathways. This can be accomplished very simply with Rigel's retroviral vector system. By using reporter genes downstream of the cDNA encoding the target protein or domain, we can track infected cells and determine the relative production of the target protein/domain. This will allow us to titrate its biological effect as a means to confirm the target protein's role in lymphocyte activation. If overexpression of the protein target influences lymphocyte activation, mutant libraries of the protein can then be screened for loss-of-function as described below.

Target proteins will be randomly mutated (see Appendix P) and screened in the FACS assays described in Section 1 for mutant proteins that alter lymphocyte activation. Two variations of this approach allow us to narrow our screen of mutant target proteins. One variation is to perform mutagenesis on the target cDNA and then subject the mutagenized target to a two-hybrid screen with the cognate peptide as bait to identify mutants that no longer bind the peptide. These mutant proteins can be tested for loss-of-function in mammalian cells. Alternatively, the peptide can be chemically crosslinked to the target protein to identify the region bound by the peptide using mass spectrometry. Subsequently, the peptide-binding region of the target protein is randomly mutated and the clones screened for their ability to inhibit lymphocyte activation. The advantage of this variation is that the regulatory domain of the target protein is identified.

A third approach to confirm the role of the target protein in lymphocyte activation is to overcome peptide inhibition by overexpressing the target protein. The screening cell lines are infected with the peptide and its target protein where the target protein under the control

of an inducible promoter such as tetracycline or metallothionein. When the target protein is induced, its ability to outcompete inhibition by the peptide can be tested.

Some or all of the above methods can be employed to confirm that a protein/peptide pair, identified in the initial screen is functionally relevant. Because of our retroviral technology virtually any strategy of intracellular expression can be utilized to verify protein/peptide target pairs in living cells. It will be the task of the RMC to determine which assays are necessary to sufficiently define a functional protein/peptide pair for the next phase of development, specifically small molecular weight compound screening.

3.2 Additional levels of Yeast two-hybrid screening to identify and map proteins that interact with the functional cDNA target

The functional cDNA targets identified in 3.1 that bind to the inhibitory peptide will be used as bait to identify its binding partners. This second level of yeast two-hybrid analysis will identify cDNA "ligands" for the target proteins identified by the inhibitory peptides. These ligands will be assessed in a variety of assess to confirm their role in the pathway leading to Ig secretion and/or B cell activation as described in 3.1.

HEADCOUNT

To run optimally, the T cell project (Project I) and the B cell project (Project II) will each take 12 full-time Rigel FTEs. Listed here are the scientists who would begin working on the B cell project (see Appendix R for an

amended list of the scientists who will begin working on the T cell project):

YING LUO: Dr. Luo is the project director and is the primary supervisor responsible for ensuring that the project hits milestones and objectives in a timely fashion. In addition, he is the head of Genomics and Target Discovery and is responsible for the supervision and data analysis resulting from YTH and HTS FACS analysis/sorting. He will also supervise all aspects of the various constructs, library generation, library enrichment steps, target validation, and target analysis.

H. MANCEBO: H. Mancebo will coordinate all communication between Rigel and Novartis. She will be responsible for the development of all primary and secondary assays for the screens. She will generate the IgH promoter survival cell lines and oversee their screening. She is responsible for analyzing the function of individual peptide and protein hits in cell lines and primary cells.

C.A. FU: Dr. Fu is a Scientist who is investigating functional B cell targets and two-hybrid hits. He is involved in developing many of the functional assays related to B cell function.

TBH: A Scientist is required who will be in charge of retroviral library design and production. The individual will be responsible for the generation of all peptide libraries with their scaffold and localization sequences. He/she will perform library rescue and the subsequent subcloning of the individual peptide hits. The individual will also shuttle hits from the yeast two-hybrid screen to mammalian vectors for post two-hybrid functional analysis.

A. FRIERA: A. Friera is the Senior Research Associate in charge of retroviral production and tissue culture. She is responsible for conducting the library screens, which involves the generation of the infectious library for each round of enrichment screening and all aspects of tissue culture associated with the screening effort. She is also coordinating and performing biological rescue to transfer enriched peptide clones from one round to the next, as well as RT-PCR isolation of individual peptide sequences.

C. YOUNG: C. Young is the Research Associate responsible for retroviral vector design and testing. He will generate the retroviral constructs to be used in all the screens. He will be responsible for performing the peptide screens and conducting the rescue of the hits from those screens. He will be involved in the screening for proteins that bind the peptide hits.

TBH: An additional cell biology Research Associate will be required who will be responsible for all the tissue culture work for the project. He will maintain all the different lymphocyte cell lines, the Phoenix packaging cell line, and the sorted cell populations.

M. FOX: M. Fox is the Research Assistant in charge of the sequencing core. He will be responsible for all DNA sequencing on this project. This includes sequencing of all rescued libraries to check for enrichment and contamination, all verified peptide hits, and two-hybrid hits. He will coordinate the data entry into the appropriate sequence databases.

ALEX ROSSI: A. Rossi is a Cell Biology Manager responsible for setting-up and implementing all the FACS-based assays. He will be responsible for adapting all assays for FACS-based sorting. He will perform these assays and sort the library hits. He will also supervise the FACS-associated bioinformatics for all the screens.

M. SHEN: M. Shen is the Senior Research Associate in charge of two-hybrid screening. She is responsible for setting up and carrying out all the two-hybrid assays, analyzing and isolating full-length clones, and generating the cDNA libraries

J. LASAGA: J. Lasaga is a molecular biology Research Associate in the target identification group. He is responsible for all the support work on the one- and two-hybrid analyses, including media prep, plate pouring, minipreps, colony picking, gel analysis, and subcloning.

RESEARCH ASSOCIATE TBH: An additional molecular biology Research Associate will be needed who will be responsible for all the subcloning of hits into expression vectors and execution of secondary assays to verify function in primary cells. This individual will also perform various labor-intensive tasks associated with the screening effort such as peptide rescue, library sequencing and tissue culture.

APPENDIX A

[DIAGRAM]

APPENDIX B

[DIAGRAM]

APPENDIX C

[DIAGRAM]

APPENDIX D

PROTOCOL FOR TRANSFECTION OF PHOENIX CELLS AND INFECTION OF NONADHERENT TARGET CELLS

[DIAGRAM]

Day 1:

Seed phoenix cells (Es or As) in 10cm plates at 5 x 10E6 cells in 6 ml (DMEM + 10% FBS + Pen/Strep) per plate the day before transfection.

Day 2:

Allow all reagents to reach room temperature 30 min. before staring. Add 50 mM chloroquine at 8 microliter/plate (50 microM final) before preparing the transfection solution.

Mix CaPO4 reagents in 15 ml polypropylene tube:

Per plate: 10 micrograms DNA
122 microliters 2M CaCl2
876 microliters H2O
1.0ml 2X HBS

Add 2X HBS and depress the expulsion button completely to bubble air through the mix for 10 secs. Immediately add mixture gently dropwise to plate. Incubate 3-8 hours.
Remove medium and replace with 6.0 ml DMEM-medium.

Day 3:

Change medium again to 6.0 mls of medium optimal for the cells to be infected. Move to 32 degrees C either in the morning of afternoon depending on the Phoenix cell confluency and whether you will infect at 48 or 72 hrs after transfection.

Day 4 or 5:

Collect virus supernatant form transfected plates (6.0 ml) into 50 ml tubes and add protamine sulfate to a final concentration of 5 micrograms/ml. Pass through a 0.45 microm filter. Count target cells and distribute 10(7) cells per 10cm plate transfected to 50 ml tubes and pellet 5 min. Resuspend each pellet of target cells in virus supernatant and transfer to a 6 well plate at 1.0-1.2 ml per well. Seal plate with parafilm and centrifuge at RT for 30-90 min. at 2500 RPM. Remove parafilm and incubate plate over night at 37 degrees C.

Day 5:

Collect and pellet each well of target cells. Resuspend in 3 ml medium and transfer back to same 6 well plate. Infection can be repeated by refeeding the Phoenix cells with 6ml fresh medium and reinfecting the same cells again up to 3 times to increase % of cells infected (for instance at 48, 56, and 72 hours)

Day 7 or Day 8:

At 48 to 72 hrs. post infection, target cells are ready to analyze for expression.

APPENDIX E

[DIAGRAM]

16.

APPENDIX F

[DIAGRAM]

17.

APPENDIX G

[DIAGRAM]

18.

APPENDIX H

[DIAGRAM]

19.

APPENDIX I

[DIAGRAM]

20.

APPENDIX J

[DIAGRAM]

21.

APPENDIX K

[DIAGRAM]

22.

APPENDIX L

[DIAGRAM]

23.

APPENDIX M

[DIAGRAM]

24.

APPENDIX N

[DIAGRAM]

25.

APPENDIX O

[DIAGRAM]

26.

APPENDIX P(1)

[DIAGRAM]

27.

APPENDIX P(2)

[DIAGRAM]

28.

APPENDIX Q1 FLOW CHART FOR FUNCTIONAL SCREENS
(IDENTIFICATION OF TARGET PROTEIN/PEPTIDE PAIRS)

[DIAGRAM]

29.

APPENDIX Q2

TARGET VALIDATION STEPS

[DIAGRAM]

30.

RIGEL/NOVARTIS COLLABORATION TIMELINE

[DIAGRAM]

31.

EXHIBIT B

<TABLE>
<CAPTION>

	PROJECT	NUMBER OF FTES	COMMENCEMENT DATE
<S>		<C>	<C>
B-1	T-Cell Project	12	Effective Date
B-2	B-Cell Project	12	To be determined

</TABLE>

EXHIBIT C

LICENCE TERMS UNDER ARTICLES 5.6 AND 6.4

1. DEFINITIONS:

For purposes of this Exhibit C the term

- - "Direct Product" shall mean a product developed by Novartis based upon a Rigel-supplied compound or a derivative thereof, the manufacture, use or sale of which in the absence of a licence, would infringe a valid claim (to be defined in a full agreement) of Rigel.

- - "Indirect Product" shall mean a product developed by Novartis based upon a Rigel-supplied compound or a derivative thereof and which is not a Direct Product.

2. CONSIDERATION DUE FOR EACH DIRECT PRODUCT:

(A) LICENSE EXECUTION AND MILESTONE PAYMENTS

Upon execution of license	$250,000
Upon start of Phase I Clinical Trials	$500,000
Upon NDA submission	$1,000,000
Upon NDA approval	$2,000,000

(B) ROYALTIES ON ANNUAL NET SALES OF DIRECT PRODUCTS DURING PATENT TERM*:

up to $300 Million	4%
on incremental sales from $300 Million to $500 Million	5%
on incremental sales from $500 Million to $750 Million	6%
on incremental sales from $750 Million to $1 Billion	7%
on incremental sales above $1Billion	8%

*subject to a deduction from royalty payments of an amount corresponding to 50% of the milestone payments made to Rigel under 2(a), provided, that each royalty payment shall not be reduced by more than 50% of the amount due prior to applying the milestone payment credit

3. CONSIDERATION DUE FOR EACH INDIRECT PRODUCTS:

- - License execution and milestone payments equal to 50% of the amounts set forth in 2.(a) above for Direct Products;

- - No royalties.

EXHIBIT D

THIRD PARTY LICENSES

Agreement between the Board of Trustees of the Leland Stanford Junior University and Rigel Pharmaceuticals, Inc. dated October 7, 1996

AGREEMENT

Effective as of October 7, 1996 ("Effective Date"), THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, a body having corporate powers under the laws of the State of California ("STANFORD") and RIGEL PHARMACEUTICALS, INC., a Delaware corporation having a principle place of business at 24 Windsor Drive, Hillsborough, CA 94010 ("RIGEL"), agree as follows:

1. BACKGROUND.

1.1 STANFORD has an assignment of U.S. Patent Application No. 08/589,109, entitled "Methods for Screening for Transdominant Effector Peptides and RNA Molecules" (the "Nolan/Rothenberg Patent Application") claiming an invention developed in the laboratory of Dr. Garry Nolan (the "Invention"), and any Licensed Patent(s), as hereinafter defined, which may claim such Invention.

1.2 STANFORD has certain biological materials and other know-how ("Know-How"), as herein defined, pertaining to the Invention.

1.3 STANFORD desires to have the Know-How and Invention perfected and marketed at the earliest possible time in order that products resulting therefrom may be available for public use and benefit.

1.4 RIGEL desires a license under said Know-How, Invention, and Licensed Patent(s) in the field of use of gene transfer technologies, including retrovirally mediated nucleic acid libraries, for drug development, drug delivery, drug screening, and target analysis and discovery associated with the development, manufacture, use and sale of Licensed product(s), as defined below.

1.5 RIGEL acknowledges that certain of the Cell Lines (as defined below) were made in the course of research supported by Progenesys.

1.6 The patent application entitled "Methods for Screening for Transdominant Intracellular Effector Peptides and RNA Molecules," which claims technology useful in the field and which was developed in the laboratory of Dr. Garry Nolan (the "Nolan Patent Application"), has previously been assigned to RIGEL.

2. DEFINITIONS.

2.1 "LICENSED BIOLOGICAL MATERIALS" means the materials listed on Exhibit A, including certain vector libraries ("Vector Libraries") and cell lines ("Cell Lines") set forth therein, as amended from time to time upon the parties' mutual written consent.

2.2 "LICENSED KNOW-HOW" means all know-how necessary or useful for the commercial exploitation of the Licensed Patents in the Licensed Field of Use, including without limitation all know-how, trade secrets, protocols, information, processes or other subject matter which is either disclosed in the Nolan/Rothenberg Patent Application, or necessary or useful to

practice the licenses granted to RIGEL in this Agreement with respect to the Invention. Licensed Know-How excludes the Licensed Patents and includes the Licensed Biological Materials.

2.3 "LICENSED PATENT(S)" means any Letters Patent, both foreign (subject to Section 7) and domestic, issued upon (i) the Nolan/Rothenberg

Patent Application (STANFORD's U.S. Patent Application Serial Number 08/589,109, filed January 23, 1996), (ii) any substitutions, divisionals, continuations, and continuations-in-part (to the extent such continuations-in-part claim subject matter disclosed in the Nolan/Rothenberg Patent Application as filed on January 23, 1996 and to the extent that the practice of an invention claimed in a Licensed Patent issuing from a patent application other than such continuation-in-part would infringe a claim of Licensed Patent issuing from such continuation-in-part), and (iii) any foreign counterparts of (i) or (ii).

2.4 "LICENSED TECHNOLOGY" means the Licensed Patent(s) and the Licensed Know-How.

2.5 "LICENSED PRODUCT(S)" means:

(a) any product, the manufacture, use, sale, offer for sale or import of which:

(1) is covered by a valid claim of an issued, unexpired Licensed Patent(s) directed to the Invention (claim of an issued, unexpired Licensed Patent(s) shall be presumed to be valid unless and until it has been held to be invalid by a final judgment of a court of competent jurisdiction from which no appeal can be or is taken), or

(2) is covered by any claim being prosecuted in a pending application directed to the Invention, which claim has not been pending for more than three (3) years from first filing of such claim;

(b) any product which directly incorporates any of the Licensed Biological Materials; or

c) any product which would not, but for the use of the Licensed Biological Materials, have been identified, discovered, or developed.

2.6 "NET SALES" means the gross revenue derived by RIGEL and/or RIGEL's sublicensee(s) from the sales of Licensed Product(s), less the following items but only insofar as they actually pertain to the disposition of such Licensed Product(s) by RIGEL or RIGEL's sublicensee(s), are included in such gross revenue, and are separately billed:

a) Import, export, excise and sales taxes, and custom duties;
b) Credit for returns, allowances, trades, or retroactive price adjustments;
c) Transportation charges, issuances and allowances;
d) Discounts actually allowed; or
e) Royalties payable to third parties on the manufacture, use, sale, offer for sale or import of Licensed Products.

2.7 "LICENSED FIELD OF USE" means the use of gene transfer technologies, including retrovirally mediated nucleic acid libraries, for drug development, drug delivery, and target

analysis and discovery. Solely with respect to the phiNX Cell Lines set forth on Exhibit A, the Licensed Field of Use excludes the use of such Cell Lines, derivatives or vectors thereof or other tangible products that are a direct lineal descendent from such Cell Lines (although obtained in any manner therefrom), wherein cells treated with any one or more of the aforementioned materials are contained within a human subject or are subsequently transplanted into a human subject.

2.8 "EXCLUSIVE" means that, subject to Article 4, STANFORD shall not grant further licenses in the Licensed Field of Use.

3. GRANT.

3.1 STANFORD hereby grants and RIGEL hereby accepts a worldwide license in the Licensed Field of Use under STANFORD's right, title and interest in the Licensed Patents and the Vector Libraries to make, use, sell, offer for sale and import Licensed Product(s).

3.2 The license granted in Section 3.1 is Exclusive, including the right to sublicense pursuant to Article 13, in the Licensed Field of Use for a term (the "Exclusivity Term") commencing as of the Effective Date and ending on the first to occur of the following:

(a) twenty (20) years from the Effective Date; or

(b) ten (10) years from the date of first commercial sale of a Licensed Product(s) by RIGEL or RIGEL's sublicensee(s). RIGEL agrees to promptly inform STANFORD in writing of the date of first commercial sale of Licensed Products. After expiration of the Exclusivity Term, said license shall become nonexclusive and continue indefinitely.

3.3 STANFORD additionally grants, and RIGEL hereby accepts, a worldwide, nonexclusive license in the Licensed Field of Use under STANFORD's right, title and interest in the Licensed Know-How other than the Vector Libraries to make, use, sell, offer for sale and import Licensed Product(s). The term of such nonexclusive license shall commence upon the Effective Date and continue indefinitely.

3.4 Notwithstanding the Exclusive license granted to RIGEL pursuant to Sections 3.1 and 3.2, STANFORD shall have the right to practice the Licensed Patents and to use the Vector Libraries for non-commercial, academic research purposes.

4. GOVERNMENT RIGHTS.

This Agreement is subject to all of the terms and conditions of Title 35 United States Code Sections 200 through 204, including an obligation that Licensed Product(s) sold or produced in the United States be "manufactured substantially in the United States," and RIGEL agrees to take all reasonable action necessary on its part as licensee to enable STANFORD to satisfy its obligation thereunder, relating to the Invention. STANFORD agrees to provide reasonable assistance to RIGEL in the event RIGEL decides to seek a waiver under such domestic manufacture requirement.

5. DILIGENCE.

5.1 As an inducement to STANFORD to enter into this Agreement, RIGEL agrees to use all reasonable efforts and diligence to proceed with the development, manufacture, and sale of Licensed Product(s) and to diligently develop markets for the Licensed Product(s). RIGEL shall demonstrate such diligence to STANFORD by achieving proof of principle through written documentation of the following within eighteen (18) months after the Effective Date:

a) Construction of a retroviral vector library;

b) Infection of cells with such vector library;

c) Detection of a physiological response to such infection in an infected cell; and

d) Isolation and analysis of the peptide eliciting such physiological response from the cell.

5.2 If RIGEL is unable to demonstrate proof of principle within eighteen (18) months after the Effective Date, STANFORD may elect to narrow the definition of the Licensed Field of Use to include only the use of retrovirally mediated nucleic acid libraries for drug development, drug delivery, drug screening, and target analysis and discovery, by providing written notice to RIGEL thereof. Additionally, RIGEL shall provide to STANFORD within eighteen (18) months after the Effective Date a plan for the development and commercialization of Licensed Products (a "Development Plan"). STANFORD shall comment upon and approve such plan, which approval shall not be unreasonably withheld. After the Development Plan is approved by STANFORD, RIGEL shall use reasonable efforts to diligently perform its obligations under such Development Plan. If Stanford reasonably believes that RIGEL is not using reasonable efforts to perform the Development Plan, STANFORD may so notify RIGEL. The parties shall promptly thereafter meet to discuss RIGEL's progress under the Development Plan, and shall develop a mutually agreeable plan for remedying any such lack of diligence (the "Proposed Remedy"). If RIGEL fails to perform the Proposed Remedy within one hundred and eighty (180) days after the Proposed Remedy is agreed upon, STANFORD may elect to narrow the definition of the Licensed Field of Use to include only the use of retrovirally mediated nucleic acid libraries for drug development, drug delivery, and target analysis and discovery by providing written notice to RIGEL. If RIGEL then fails to perform the Proposed Remedy within ninety (90) days after receiving STANFORD's notice that it has elected to so narrow the Licensed Field of Use definition, then STANFORD may elect to convert the Exclusive License granted to RIGEL pursuant to Sections 3.1 and 3.2 to a nonexclusive license for the remaining term of this Agreement.

5.3 PROGRESS REPORT. On or before each anniversary of the Effective Date until RIGEL markets a Licensed Product(s), RIGEL shall make a written annual report to STANFORD covering RIGEL's progress during the preceding year toward commercial use of Licensed Product(s). Such report shall include, as a minimum, information sufficient to enable STANFORD to satisfy relevant reporting requirements of the U.S. Government and to ascertain progress by RIGEL toward meeting the diligence requirements of this Article 5.

6. ROYALTIES.

6.1 RIGEL agrees to pay to STANFORD a noncreditable, nonrefundable license issue royalty of Twenty Thousand Dollars ($20,000) half of which shall be paid within forty-five (45) days after the Effective Date and the balance of which shall be on the first anniversary of the Effective Date.

6.2 Upon each anniversary of the Effective Date, RIGEL shall also pay to STANFORD a Minimum Annual Royalty as follows:

Anniversary of Effective Date	Minimum Annual Royalty Due
First and Second	$10,000
Third through Seventh	$20,000
Eighth and Thereafter	$40,000

Said Minimum Annual Royalty payments are nonrefundable but they are creditable against earned royalties to the extent provided in Paragraph 6.5. The foregoing Minimum Annual Royalty payment shall be decreased by fifty percent (50%) if either:

(i) Stanford abandons all patent applications from which Licensed Patent(s) could issue prior to the time that any Licensed Patent(s) issue; or

(ii) Stanford elects to narrow the definition of the Licensed Field of Use pursuant to Section 5.2.

6.3 If Rigel grants to a third party a sublicense under the Licensed Technology solely for research, and not commercialization purposes (a "Research Sublicense"), Rigel shall also pay to STANFORD a milestone payment equal to one percent (1%) of any research milestone payment that RIGEL receives as consideration for the grant of such Research Sublicense. RIGEL shall pay such amount to STANFORD within sixty (60) days after RIGEL receives such research milestone payment.

If RIGEL grants to a third party a sublicense under the Licensed Technology which includes the right to sell and offer for sale Licensed Products (a "Commercialization Sublicense"), RIGEL shall pay to STANFORD a sublicense fee as follows:

First Sublicense Granted	$10,000
Second Sublicensed Granted	$20,000
Each Additional Sublicense Granted	$30,000

RIGEL shall pay such sublicense fees to STANFORD within sixty (60) days after the effective date of each Commercialization Sublicense.

6.4 In addition, RIGEL shall pay STANFORD earned royalties equal to (i) 0.5% of Net Sales of Licensed Products set forth in Sections 2.5(a) and 2.5(b), or 0.25% of Net Sales of Licensed Products which can only be categorized under Section 2.5(c). If a Licensed product

can be included in more than one of Sections 2.5(a), 2.5(b) or 2.5(c), the royalty rate due to STANFORD on Net Sales of such Licensed Product shall be 0.5%.

6.5 As further consideration for the license granted to RIGEL under this Agreement, RIGEL shall issue to STANFORD forty thousand (40,000) shares of Preferred Stock of RIGEL, pursuant to a Stock Purchase Agreement. If such number of shares shall equal less than three tenths of one percent (0.3%) of the total outstanding shares of RIGEL's stock at any time during the period from the date of issuance of such stock until one (1) year thereafter, STANFORD and RIGEL shall discuss whether RIGEL shall adjust the number of shares issued to Stanford under this Section 6.5.

6.6 Creditable payments under this Agreement shall be an offset to RIGEL against up to fifty percent (50%) of each earned royalty payment which RIGEL would be required to pay pursuant to Paragraph 6.4 until the entire credit is exhausted.

6.7 If this Agreement is not terminated in accordance with other provisions hereof, RIGEL's obligation to pay royalties hereunder shall continue until ten (10) years after first commercial sale of Licensed Products.

6.8 The royalty on sales in currencies other than U.S. Dollars shall be calculated using the appropriate foreign exchange rate for such currency quoted by the Bank of America (San Francisco) foreign exchange desk, on the close of business on the last banking day of each calendar quarter. Royalty payments to STANFORD shall be in U.S. Dollars. All non-U.S. taxes related to royalty payments shall be paid by RIGEL and are not deductible from the payments due STANFORD.

6.9 Within thirty (30) days after receipt of a statement from STANFORD,

RIGEL shall reimburse STANFORD for all costs incurred by STANFORD, including those costs incurred prior to the Effective Date, in connection with the preparation, filing and prosecution of all patent applications and maintenance of patents corresponding to the Invention.

7. PATENT RIGHTS.

STANFORD shall have the obligation to file, prosecute and maintain all patent applications and patents included in the Licensed Patents. STANFORD will provide RIGEL with an opportunity to review and comment upon the prosecution strategy and to consult with STANFORD on the content of patent filings, and will provide copies of any correspondence relating to patent applications and patents included in the Licensed Patents to RIGEL or a designee of RIGEL. RIGEL shall have the right to designate, in its sole discretion, those foreign countries in which STANFORD will file, prosecute and maintain patents and patent applications included in the Licensed Patents. STANFORD may propose to file, prosecute and maintain a Licensed Patent in a country which RIGEL has not designated pursuant to this Section 7. If RIGEL agrees to such designation, it shall reimburse STANFORD costs of such filing, prosecution of maintenance of such patent or patent applications pursuant to Section 6.9 and such patent or patent applications shall be included in the Licensed Patents. If RIGEL does not agree to such proposal, STANFORD may elect to proceed with such filing, prosecution or

maintenance at its own expense, and such patent or patent applications shall not be included in the Licensed Patents.

8. ROYALTY REPORTS, PAYMENTS, AND ACCOUNTING.

8.1 QUARTERLY EARNED ROYALTY PAYMENT AND REPORT. Beginning with the first sale of a Licensed Product, RIGEL shall make written reports (even if there are no sales) and earned royalty payments to STANFORD within thirty (30) days after the end of each calendar quarter. This report shall be in the form of the report of Appendix B and shall state the number, description, and aggregate Net Sales of Licensed Product(s) during such completed calendar quarter, and resulting calculation pursuant to Paragraph 6.4 of earned royalty payment due STANFORD for such completed calendar quarter. Concurrent with the making of each such report, RIGEL shall include payment due STANFORD of royalties for the calendar quarter covered by such report.

8.2 ACCOUNTING. RIGEL agrees to keep and maintain records for a period of three (3) years showing the manufacture, sale, use, and other disposition of products sold or otherwise disposed of under the license herein granted. Such records will include general ledger records showing cash receipts and expenses, and records which include production records, customers serial numbers and related information in sufficient detail to enable the royalties payable hereunder by RIGEL to be determined. RIGEL further agrees to permit its books and records to be examined by STANFORD from time to time to the extent necessary to verify reports provided for in Paragraph 8.1. Such examination is to be made by STANFORD or its designee, at the expense of STANFORD, except in the event that the results of the audit reveal an underreporting of royalties due STANFORD of five percent (5%) or more, then the audit costs shall be paid by RIGEL.

9. NEGATION OF WARRANTIES.

9.1 Nothing in this Agreement is or shall be construed as:

a) A warranty or representation by STANFORD as to the validity or scope of any Licensed Patent(s);

b) A warranty or representation that anything made, used, sold, or otherwise disposed of under any license granted in this Agreement is or will be free from infringement of patents, copyrights, and other rights of third parties;

c) An obligation to bring or prosecute actions or suits against third parties for infringement, except to the extent and in the circumstances described in Article 13;

d) Granting by implication, estoppel, or otherwise any licenses or rights under patents or other rights of STANFORD or other persons other than Licensed Patent(s), regardless of whether such patents or other rights are dominant or subordinate to any Licensed Patent(s); or

e) An obligation to furnish any technology or technological information other than the Licensed Technology.

9.2 Except as expressly set forth in the Agreement STANFORD MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR

FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE LICENSED PRODUCT(S) WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER RIGHTS, OR ANY OTHER EXPRESS OR IMPLIED WARRANTIES.

9.3 RIGEL agrees that nothing in this Agreement grants RIGEL any express or implied license or right under or to:

a) U.S. Patent No. 4,237,224, "Process for Producing Biologically Functional Molecular Chimeras"; U.S. Patent No. 4,468,464 and U.S. Patent No. 4,740470, both entitled, "Biologically Functional Molecular Chimeras" (collectively known as the Cohen/Boyer patents), or reissues thereof; or

b) U.S. Patent 4,656,134 "Amplification of Eucaryotic Genes" or any patent application corresponding thereto.

9.4 STANFORD warrants that it has all right, power and authority necessary to grant the licenses set forth in Article 3 to RIGEL, and that it has not, and will not during the term of this Agreement, grant any right to any third party which would conflict with the rights granted to RIGEL hereunder.

10. INDEMNITY.

10.1 RIGEL agrees to indemnify, hold harmless, and defend STANFORD and Stanford Health Services and their respective trustees, officers, employees, students, and agents against any and all claims by third parties for death, illness, personal injury, property damage, and improper business practices arising out of the manufacture, use, sale, or other disposition of the Invention, Licensed Technology, or Licensed Product(s) by RIGEL or RIGEL's sublicensee(s) or customers.

10.2 STANFORD shall not be liable for any indirect, special, consequential or other damages whatsoever, whether grounded in tort (including negligence), strict liability, contract or otherwise. STANFORD shall not have any responsibilities or liabilities whatsoever with respect to Licensed Product(s).

10.3 RIGEL shall at all times comply, through insurance or self-insurance, with all statutory workers' compensation and employers' liability requirements covering any and all employees with respect to activities performed under this Agreement.

10.4 In addition to the foregoing, RIGEL shall maintain Comprehensive General Liability Insurance, with reputable and financially secure insurance carrier(s) to cover the activities of RIGEL and its sublicensee(s) in the amounts and during the periods specified herein. Such insurance shall provide minimum limits of liability of One Million Dollars ($1,000,000) as of the first anniversary of the date upon which RIGEL first leases a facility in which it will

conduct research and development activities, and of Five Million Dollars ($5,000,000) as of the commencement of human clinical trials of Licensed Products. Such insurance shall include STANFORD, Stanford Health Services, their trustees, directors, officers, employees, students, and agents as additional insureds. Such insurance shall be written to cover claims incurred, discovered, manifested, or made during or after the expiration of this Agreement. At STANFORD's request, RIGEL shall furnish a Certificate of Insurance evidencing primary coverage and requiring thirty (30) days prior written notice of cancellation or material change to STANFORD. RIGEL shall advise STANFORD, in writing, that it maintains excess liability coverage (following form) over primary insurance for at least the minimum limits set forth above. All such insurance of RIGEL shall be primary coverage; insurance of STANFORD or Stanford Health Services shall be excess and noncontributory.

11. MARKING.

Prior to the issuance of patents on the Invention, RIGEL agrees to mark Licensed Product(s) (or their containers or labels) made, sold, or otherwise disposed of by it under the licenses granted in this Agreement with the words "Patent Pending," and following the issuance of one or more patents, with the numbers of the Licensed Patent(s).

12. STANFORD NAMES AND MARKS.

RIGEL agrees not to identify STANFORD in any promotional advertising or other promotional materials to be disseminated to the pubic or any portion thereof or to use the name of any STANFORD faculty member, employee, or student or any trademark, service mark, trade name, or symbol of STANFORD or the Stanford University Hospital, or that is associated with either of them, without STANFORD's prior written consent, except as required by law. STANFORD shall not unreasonably hold consent under this Section 12.

13. INFRINGEMENT BY OTHERS: PROTECTION OF PATENTS.

13.1 RIGEL shall promptly inform STANFORD of any suspected infringement of any Licensed Patent(s) by a third party. During the Exclusive period of this Agreement, STANFORD and RIGEL each shall have the right to institute an action for infringement of the Licensed Patent(s) against such third party in accordance with the following:

a) If STANFORD and RIGEL agree to institute suit jointly, the suit shall be brought in both their names, the out-of-pocket costs thereof shall be borne equally, and any recovery or settlement shall be shared equally. RIGEL and STANFORD shall agree to the manner in which they shall exercise control over such action. STANFORD may, if it so desires, also be represented by separate counsel of its own selection, the fees for which counsel shall be paid by STANFORD;

b) In the absence of agreement to institute a suit jointly, STANFORD may institute suit, and, at its option, join RIGEL as a plaintiff. If STANFORD decides to institute suit, then it shall notify RIGEL in writing. STANFORD shall bear the entire cost of such litigation and shall be entitled to retain the entire amount of any recovery or settlement; and

c) In the absence of agreement to institute a suit jointly and if STANFORD notifies RIGEL that it has decided not to join in or institute a suit, as provided in (a) or (b) above, RIGEL may institute suit and, at its option, join STANFORD as a plaintiff. RIGEL shall bear the entire cost of such litigation and shall be entitled to retain the entire amount of any recovery or settlement, provided, however, that any recovery in excess of litigation costs shall be deemed to be Net Sales, and RIGEL shall pay STANFORD royalties thereon at the rates specified herein.

13.2 Should either STANFORD or RIGEL commence a suit under the provisions of Paragraph 13.1 and thereafter elect to abandon the same, it shall give timely notice to the other party who may, if it so desires, continue prosecution of such suit, provided, however, that the sharing of expenses and any recovery in such suit shall be as agreed upon between STANFORD and RIGEL.

14. SUBLICENSE(S).

14.1 RIGEL may grant sublicense(s) under its Exclusive license rights during the Exclusivity Term. RIGEL may grant sublicense(s) under nonexclusive license rights, if such sublicense is in conjunction with a sublicense of other RIGEL proprietary technology.

14.2 If RIGEL is unable or unwilling to serve or develop a potential market or market territory for which there is a willing sublicense(s), RIGEL will, at STANFORD's request negotiate in good faith a sublicense(s) hereunder on commercially reasonable terms.

14.3 Any sublicense(s) granted by RIGEL under this Agreement shall be subject and subordinate to terms and conditions of this Agreement, except:

a) Sublicense terms and conditions shall reflect that any sublicensee(s) shall not grant a sublicense to a third party; and

b) The earned royalty rate specified in the sublicense(s) may be at higher rates than the rates in this Agreement.

Any such sublicense(s) also shall expressly include the provisions of Articles 8, 9, and 10 for the benefit of STANFORD and provide for the transfer of all obligations including the payment of royalties specified in such sublicense(s), to STANFORD or its designee, in the event that this Agreement is terminated.

14.4 RIGEL agrees to provide STANFORD a copy of any sublicense(s) granted pursuant to this Article 14.

15. TERMINATION.

15.1 RIGEL may terminate this Agreement by giving STANFORD notice in writing at least thirty (30) days in advance of the Effective Date of termination selected by RIGEL.

15.2 STANFORD may terminate this Agreement if RIGEL:

a) Is in default in payment of royalty or providing of reports;

b) Is in material breach of any provision hereof; or

c) Intentionally provides any false report;

and RIGEL fails to remedy any such default, breach, or false report within thirty (30) days after written notice thereof by STANFORD.

15.3 Surviving any termination are:

a) RIGEL's obligation to pay royalties accrued or accruable;

b) Any cause of action or claim of RIGEL or STANFORD, accrued or to accrue, because of any breach or default by the other party; and

c) The provisions of Articles 8, 9, and 10.

16. ASSIGNMENT.

This Agreement may not be assigned by either party without the express written consent of the other party, except that RIGEL may assign the Agreement in connection with a merger, consolidation or sale of all or substantially all of RIGEL's assets.

17. DOUBLE PATENTING CONTINGENCY.

If the PTO rejects the claims of the Nolan/Rothenberg Patent Application for double patenting in view of the claims of the Nolan Patent Application, or the claims of the Nolan Patent Application for double patenting in view of the claims of the Nolan/Rothenberg Patent Application, then RIGEL may elect to assign its right, title and interest in the Nolan Patent Application to STANFORD, in which case STANFORD shall grant to RIGEL an irrevocable, exclusive, worldwide, royalty-free license under STANFORD's right, title and interest in the Nolan Patent Application for all purposes.

18. ARBITRATION.

18.1 Any controversy arising under or related to this Agreement, and any disputed claim by either party against the other under this Agreement excluding any dispute relating to patent validity or infringement arising under this Agreement, shall be settled by arbitration in accordance with the Licensing Agreement Arbitration Rules of the American Arbitration Association.

18.2 Upon request by either party, arbitration will be by a third party arbitrator mutually agreed upon in writing by RIGEL and STANFORD within thirty (30) days of such arbitration request. Judgement upon the award rendered by the arbitrator shall be final and nonappealable and may be entered in any court having jurisdiction thereof.

18.3 The parties shall be entitled to discovery in like manner as if the arbitration were a civil suit in the California Superior Court.

18.4 Any arbitration shall be held at Stanford, California, unless the parties hereto mutually agree in writing to another place.

19. NOTICES.

All notices under this Agreement shall be deemed to have been fully given when done in writing and deposited in the United States mail registered or certified, and addressed as follows:

To STANFORD: Office of Technology Licensing
Stanford University
900 Welch Road, Suite 350
Palo Alto, CA 94304-1850

Attention: Director

To RIGEL: 24 Windsor Drive
Hillsborough, CA 94010

Attention: Dr. Donald G. Payan

Either party may change its address upon written notice to the other party.

20. WAIVER

None of the terms of this Agreement can be waived except by the written consent of the party waiving compliance.

21. APPLICABLE LAW.

This Agreement shall be governed by the laws of the State of California applicable to agreements negotiated, executed and performed wholly within California.

22. SEVERABILITY.

If any provision or provisions of this Agreement shall be held to be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not be in any way affected or impaired thereby.

23. ENTIRE AGREEMENT.

This Agreement, together with the Exhibits attached hereto, embodies the entire understanding of the parties and shall supercede all previous communications, representations or understandings, either oral or written, between the parties relating to the subject matter hereof. No amendment or modification hereof shall be valid or binding upon the parties unless made in writing and signed by duly authorized representatives of both parties.

24. COUNTERPARTS.

This Agreement may be executed in counterparts, with the same force and effect as if the parties had executed the same instrument.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement in duplicate originals by their duly authorized officers or representatives.

THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY

Signature /s/ Katherine Ku

Name Katherine Ku

Title Director, Technology Licensing

Date October 7, 1996

RIGEL PHARMACEUTICALS, INC.

Signature /s/ Donald G. Payan

Name Donald G. Payan

Title President & CEO

Date 10/9/96

EXHIBIT A

MATERIALS FROM NOLAN LAB TO BE LICENSED TO RIGEL

Vector Libraries

1. Random peptide library in pMSCU & Bst X1
2. SH-3 first generation library
3. CPP32 inhibitor peptide library
4. SH-3 second generation library
5. Coiled-coil library

Plasmids

1. pMSCU SD & Bst X1
2. pBabc Pur
3. pMSCU SD - IRES neo Bst X1
4. p5 & MD

Cell Lines

1. phiNX cell lines - gp, eco, ampho
2. 293 T

EXHIBIT B

SAMPLE REPORTING FORM

Stanford Docket No. S_____-_____

This report is provided pursuant to the license agreement between Stanford University and _____.

License Agreement Effective Date: _____

Report Covering Period	_____
Fixed Fees (Annual Minimum Payment)	$_____
Number of Sublicenses Executed	_____
Net Sales	$_____
Royalty Calculation	_____
Royalty Subtotal	$_____
Credit	$_____
Royalty Due	$_____

Comments:

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY BRACKETS, HAS BEEN OMITTED AND FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 OF THE SECURITIES ACT OF 1933, AS AMENDED.

EXHIBIT 10.9

LICENSE AND RESEARCH AGREEMENT

THIS LICENSE AND RESEARCH AGREEMENT (the "Agreement") is made and entered into as of 2 September, 1999, (the "Effective Date") by and between Rigel Pharmaceuticals, Inc., a corporation organized under the laws of Delaware and having a principal place of business at 240 East Grand Avenue, South San Francisco, CA 94080 ("Rigel") and Cell Genesys, Inc. a corporation organized under the laws of Delaware and having a principal place of business at 342 Lakeside Drive, Foster City, CA 94404 ("CG"). Rigel and CG may be referred to collectively as the "Parties," or individually as a "Party."

RECITALS

WHEREAS, CG owns patents relating to [*] cell lines [*] and [*] cell lines (Rockefeller), and related technology; and

WHEREAS, Rigel has a license to the [*] cell lines, associated vectors and vector libraries under intellectual property rights owned by Stanford University; and

WHEREAS, CG and Rigel desire to enter into an agreement granting each other licenses under such patents and other intellectual property rights as provided herein; and

WHEREAS, Rigel is in the business of, among other things, providing services for identifying molecules which bind together in intracellular signaling pathways, and CG desires that Rigel perform such services for CG to identify peptides, proteins and/or Genetic Material (as defined below) that modulate angiogenesis in endothelial tissues.

NOW THEREFORE, in consideration of the foregoing premises and the covenants and promises contained in this Agreement, the Parties agree as follows:

ARTICLE 1

DEFINITIONS

1.1 "AFFILIATE" shall mean, with respect to a Party to this Agreement, any other entity, whether de jure or de facto, which directly or indirectly controls, is controlled by, or is under common control with, such Party. A business entity or Party shall be regarded as in control of another business entity if it owns, or directly or indirectly controls, at least fifty percent (50%) (or such lesser percentage which is the maximum allowed to be owned by a foreign entity in a particular jurisdiction) of the voting stock or other ownership interest of the other entity, or if it

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directly or indirectly possesses the power to direct or cause the direction of the management and policies of the other entity by any lawful means whatsoever.

1.2 "CG COLLABORATION PARTNERS" means those third parties which enter into a research or development agreement with CG under which CG conducts substantial research or development activities in collaboration with such third party and grants a license to such third party under patents and/or know-how owned or controlled by CG in addition to a sublicense under the Rigel Biological Materials or Rigel Know-How, which licenses and sublicense are for the further development and commercialization of the results of such collaborative research or development.

1.3 "CG [*] FIELD" means human Gene Therapy and animal Gene Therapy.

1.4 "CG KNOW-HOW" means all Information Controlled by CG as of the Effective Date that is necessary or useful for practicing the CG Patents.

1.5 "CG LICENSE" means the license agreement between CG and Rockefeller University as in effect as of the Effective Date and attached hereto as

Appendix A.

1.6 "CG PATENTS" means the Patents and applications listed on Appendix B, to the extent the same as Controlled by CG.

1.7 "CG PROGRAM FIELD" means the research, development or commercialization of human or animal therapeutic products and services, which products and/or services are comprised of peptides, proteins or Gene Therapy.

1.8 "CONTROL" OR "CONTROLLED" means ownership of, or a license to, a particular item, material or intellectual property right with the ability to grant to the other Party access to and/or a license or sublicense as provided for herein without violating the terms of any agreement with a Third Party under which such rights were acquired from such Third Party.

1.9 "FIELD OF RESEARCH" means identification of peptides, proteins and/or Genetic Material that modulate angiogenesis in endothelial tissues.

1.10 "FTE" means a full-time employee or consultant of Rigel or the equivalent thereof.

1.11 "FTE YEAR" means the amount of time one FTE would spend working during one (1) calendar year.

1.12 "GENE THERAPY" means a product or service for the treatment or prevention of a disease that utilizes ex vivo or in vivo delivery (via viral or nonviral gene transfer methods or systems) of Genetic Material, including any cell incorporating Genetic Material.

1.13 "GENETIC MATERIAL" means a nucleotide sequence, including DNA, RNA and complementary and reverse complementary nucleotide sequences thereto, whether coding or noncoding and whether intact or a fragment.

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1.14 "INFORMATION" means any and all information, including without limitation techniques, inventions, practices, methods, knowledge, know-how, skill, experience, test data, analytical and quality control data, compositions and assays, and any business, marketing, personnel or financial information or matters.

1.15 "PATENT" means an issued, valid, unexpired patent, including any extension, registration, confirmation, reissue, re-examination or renewal thereof, or a pending application for a patent, in any country, region or jurisdiction.

1.16 "PROGRAM KNOW-HOW" shall mean any Information developed in the Research relating to the development of Therapeutic Candidates, excluding Information relating to Targets.

1.17 "PROGRAM PATENT" shall mean a Patent claiming inventions or discoveries in the Program Know-How.

1.18 "PROGRAM TECHNOLOGY" shall mean Program Know-How and Program Patents.

1.19 "RESEARCH" shall have the meaning provided in Section 3.1(a).

1.20 "RESEARCH PLAN" shall have the meaning provided in Section 3.1(a).

1.21 "RIGEL BIOLOGICAL MATERIALS" means the [*] cell lines, associated vectors and vector libraries set forth in Appendix C.

1.22 "RIGEL COLLABORATION PARTNERS" means those third parties which enter into a research or development agreement with Rigel under which Rigel conducts substantial research or development activities in collaboration with such third party and grants a license to such third party under patents and/or know-how owned or controlled by Rigel in addition to a sublicense under CG Patents and/or CG Know-How, which licenses and sublicense are for the further development and commercialization of the results of such collaborative research or development.

1.23 "RIGEL FIELD" means the creation and use of virally produced peptide and protein libraries for the screening of transdominant effector peptides and RNA molecules as claimed in the patent applications set forth on Appendix D as well as any processes, techniques and applications disclosed in the foregoing patents applications; it is understood that the foregoing technology is to be used for (a) the discovery, validation and development of targets for human or animal therapeutics, and (b) the discovery, testing, development and commercialization of therapeutic, diagnostic and drug

delivery products. For purposes of this Section 1.23, "disclosed in" shall mean disclosed in the specifications of such patent applications as necessary to practice the invention claimed and not solely as part of the description of the prior art.

1.24 "RIGEL KNOW-HOW" means all Information Controlled by Rigel as of the Effective Date necessary or useful for the use or modification of the Rigel Biological Materials.

1.25 "RIGEL LICENSE" means the license agreements between Rigel and Stanford University as in effect as of the Effective Date and attached hereto as Appendix E.

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1.26 "RMC" shall have the meaning provided in Section 3.2.

1.27 "SUCCESS CRITERIA" shall have the meaning provided in Section 3.1(b).

1.28 "TAIL END PERIOD" shall mean the period of six (6) months after the end of the Research Period, the purpose of which is to permit the RMC to identify Therapeutic Candidates; provided, however, that if this Agreement is terminated prior to or during the Tail End Period, the Tail End Period shall be deemed to end upon such termination date.

1.29 "TARGET" shall mean a molecule occurring naturally in the body that is shown during the Research to directly or indirectly cause or impede angiogenesis in endothelial tissue, to the extent such molecule (or its binding to another molecule) is agonized or antagonized by a Therapeutic Candidate. It is understood that a particular protein, peptide of Genetic Material could be both a Therapeutic Candidate and a Target, and in such case such molecule shall be treated as a "Target" hereunder to the extent that such molecule is used as a drug discovery target, and shall at the same time be treated as a "Therapeutic Candidate" hereunder to the extent such molecule is used as a drug or therapy.

1.30 "THERAPEUTIC CANDIDATE" shall mean a peptide, protein or Genetic Material discovered, identified, produced or tested during the Research Period pursuant to the Research, or identified during the Tail End Period, which meets the Success Criteria, and any homologues or derivatives thereof. For such purposes, it is understood that if a protein or peptide meets the Success Criteria, Genetic Material that codes for such protein or peptide (or its homologues or derivatives) shall be within the definition of Therapeutic Candidate (and vice-versa).

1.31 "[*] PATENTS" means the patents listed in Appendix F.

ARTICLE 2

LICENSES

2.1 CG LICENSE GRANTS.

(a) Subject to the terms of license of the CG License, CG hereby grants to Rigel a royalty-free, non-exclusive, worldwide license, with the right to sublicense to Rigel Collaboration Partners, under and to CG's right, title and interest in any Program Technology owned solely by CG, all for purposes solely within the Rigel Field; and hereby waives any claims against Rigel for the practice and use of the CG Patents and CG Know-How within the Rigel Field prior to the Effective Date. Any sublicense granted hereunder to Rigel Collaboration Partners shall be limited to the purposes of such collaboration (as such purposes are described in Section 1.22 above).

(b) CG hereby grants to Rigel a royalty-free, exclusive, worldwide license, with the right to grant and authorize sublicenses, under CG's right, title and interest in the Program Technology that is owned jointly by the Parties under Section 4.1(d) below, and Targets

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that are similarly owned jointly with Rigel, all to make and use the Targets for purposes outside the CG Program Field.

(c) CG has entered into a license agreement with the [*] concerning the [*] Patents which includes the right to sublicense (the "[*] Agreement"); as of the Effective Date, however, the terms under which CG may grant sublicenses under the [*] Agreement make impractical a sublicense to Rigel under the [*] patents for purposes of the Rigel Field. In the event that CG successfully renegotiates the terms of the [*] Agreement such that such sublicense would be practical, CG agrees to discuss in good faith the grant of a sublicense to Rigel under the [*] patents. The Parties understand and agree, however, that CG is not and shall not be obligated to enter into any agreement with Rigel concerning the [*] Patents, that failure to reach such an agreement for any reason shall not be deemed a breach of this Agreement and that this Section 2.1(C) shall not be deemed to preclude CG form entering into an agreement with a third party of any type or at any time concerning the [*] Patents.

2.2 RIGEL LICENSE GRANTS.

(a) Subject to the terms and prior to the termination or expiration of the Rigel License, the Parties agree that Rigel shall grant to CG, at CG's sole option and upon CG's request, a royalty-free, non-exclusive, worldwide license, without the right to sublicense, under Rigel's right, title and interest in the Rigel Know-How and Rigel Biological Materials, to make, have made, use sell, offer for sale and import products in the CG [*] Field. It is understood that in no event will CG have any obligation to obtain such license from Rigel. Rigel will give CG thirty (30) days prior written notice of the termination of the Rigel License by Rigel.

(b) Rigel hereby grants to CG:

(i) a royalty-free, exclusive, world-wide license, with the right to grant and authorize sublicenses, under Rigel's right, title and interest in the Program Technology (including without limitation the Therapeutic Candidates) owned solely by Rigel or jointly with CG, to make, have made, use, sell, offer for sale and import products, and otherwise exploit the Program Technology, in each case for purposes solely within the CG Program Field; and

(ii) subject to rights previously granted to third parties, a royalty-free, non-exclusive, worldwide license, with the right to grant sublicenses, under Rigel's right, title and interest in and to all Patents with priority dates prior to the Effective Date that claim Therapeutic Candidates, or the manufacture or use thereof, to make, have made, use and sell products in Gene Therapy incorporating such Therapeutic Candidates.

(c) In addition, Rigel hereby grants to CG a royalty-free, non-exclusive license, without the right to sublicense to CG Collaboration Partners, under Rigel's right, title and interest in the Targets to make and use the Targets solely for the research and development of Therapeutic Candidates in the Field of Research. For clarity, it is understood and agreed that the licenses granted to CG under this Section 2.2 specifically exclude the performance by CG of research on or with a Target which is outside the Field of Research. Any sublicense granted hereunder to CG Collaboration Partners shall be limited to the purposes of such collaboration.

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2.3 RIGEL COVENANT. Rigel hereby covenants that neither Rigel nor its Affiliates will make any claims against CG, its permitted sublicensees, distributors and customers in the chain of title with CG or its permitted sublicensees for Patent infringement as a result of activities which are explicitly permitted under the terms of this Agreement, nor shall Rigel or its Affiliates authorize a third party to make such a claim, and Rigel agrees to cooperate with CG in the defense against any such claim by licensees of Rigel.

2.4 NO OTHER LICENSE. No right or license is granted by either Party to the other under any other intellectual property other than those items expressly included in the licenses granted in this Article 2. Accordingly, no license shall be deemed granted by implication, estoppel or otherwise, if such license is not expressly and specifically granted in this Article 2.

ARTICLE 3

RESEARCH

3.1 RESEARCH.

(a) Rigel agrees to (i) use diligent efforts to conduct research within the Field of Research (the "Research"), in accordance with the research plan (the "Research Plan") incorporated hereby in, and appended to, this Agreement as Appendix G, as amended from time to time by written agreement of the Parties; and (ii) use diligent efforts to meet the goals of the Research Plan according to the timetables set forth therein. Without limiting the foregoing, the Research shall commence on the Effective Date and terminate upon the earlier of three (3) years after the Effective Date or the termination of the Agreement (the "Research Period"). Rigel will commit [*] during each year of the Research Period, or such other allocation as the RMC may decide, provided that in the event the RMC decides to reallocate FTEs between years, Rigel shall have no obligation to commit more than [*] in total over the entire Research Period. The individual FTEs who will conduct the Research are listed in Appendix H and may be replaced by Rigel, as reasonably agreed by the Parties, with other FTEs of comparable skill and expertise. Rigel agrees to test against the Success Criteria during the Research Period any proteins, peptides and Genetic Material produced or evaluated in connection with the Research as contemplated in the Research Plan.

(b) The Parties shall reasonably establish criteria for determining whether a particular peptide, protein or Genetic Material modulates angiogenesis in endothelial tissue in assays performed at Rigel, as such criteria are contemplated in the Research Plan (the "Success Criteria").

3.2 RESEARCH MANAGEMENT COMMITTEE. The Parties shall form a research management committee (the "RMC") comprised of four (4) individuals, two (2) being Rigel employees appointed and replaced by Rigel at its discretion, and two (2) being CG employees appointed and replaced by CG at its discretion. The size and composition of the RMC may be modified by mutual agreement of the Parties. The RMC shall evaluate the results of the Research set forth in the research reports pursuant to Section 3.4(a) to assess whether a peptide, protein or

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Genetic Material is a Therapeutic Candidate, and perform such other duties as specifically delegated to the RMC by mutual written agreement of the Parties.

3.3 RMC MEETINGS AND ACTIONS. RMC Meetings shall take place at such times and places as shall be determined by the RMC in order for the RMC to fulfill its obligations under Section 3.2. It is expected that the meetings will alternate between appropriate offices of each Party, or at such other convenient locations as agreed. If agreed by its members, the RMC may conduct meetings by telephone or video conference or other acceptable electronic means, provided that any decisions made during such meeting are recorded in writing and confirmed by signature of at least one (1) of the RMC members from each of the Parties. All decisions of or actions taken by the RMC shall be by unanimous approval of all the members of the RMC, and voting on any matters shall be reflected in the minutes of the meeting at which the vote was taken. If the RMC is unable to reach unanimous decision on any particular matter or issue, such matter or issue shall be referred to the chief executive officer of each Party or their designees for resolution. It is understood that for purposes of determining the Parties' rights and obligations under this Agreement, the authority of the RMC shall be limited to deciding those specific issues specifically delegated to the RMC in other Articles of this Agreement (i.e., other than the general matters described in this Article 3).

3.4 REPORTS; DISCLOSURE.

(a) Rigel shall keep CG fully informed of the progress and results of the Research and shall provide written reports at or before each RMC meeting describing its activities, the level of effort applied to, and the results of, the Research, specifically including Rigel's determination as to which peptides, proteins or Genetic Material as of the date of such report meet the Success Criteria. Such RMC reports shall be in such form and contain such detail as the RMC shall determine. Rigel agrees to fully disclose to CG the Program Technology and the Targets, and to provide CG with reasonable quantities of Targets and Therapeutic Candidates generated or utilized in connection with the Research.

(b) Rigel agrees to maintain records of its activities in performing the Research, in good scientific manner, and to permit CG to have access to such records upon ten (10) days written notice to Rigel and during regular business hours, to the extent reasonably necessary to verify that Rigel has met its obligations under this Section 3.4.

3.5 EXCLUSIVITY OF EFFORTS. Rigel agrees that neither Rigel nor any of

its Affiliates shall directly or indirectly conduct or sponsor any research, develop or otherwise commercialize any products or technologies within the Field of Research, other than pursuant to the Research Plan, during the Research Period and for a period of one (1) year following the Research Period. Without limiting the foregoing, Rigel shall not appoint or license any third party to develop market, sell or otherwise distribute such products until after the expiration of one (1) year following the Research Period.

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ARTICLE 4

INTELLECTUAL PROPERTY MATTERS

4.1 OWNERSHIP AND PROSECUTION. Subject to the terms of this Agreement, as between the Parties hereto:

(a) It is understood that CG retains its entire right, title and interest in the CG Patents and CG Know-How, subject only to the rights expressly granted to Rigel hereunder, and shall have the right, but not the obligation, to file, prosecute and maintain any Patents related thereto at its expense.

(b) It is understood that Rigel retains its entire right, title and interest in the Rigel Biological Materials and Rigel Know-How, subject only to the rights expressly granted to CG hereunder, and shall have the right, but not the obligation, to file, prosecute and maintain any Patents related thereto at its expense.

(c) It is understood that, subject only to the rights expressly granted to the other Party hereunder, each Party retains its entire right, title and interest in and to any inventions, discoveries, know-how, trade secrets, and other information made or developed solely by such Party and/or its consultants in the course of the performance of this Agreement ("Sole Inventions"), and, subject to subsection (e) below, shall have the right, but not the obligation, to file, prosecute and maintain any Patents claiming its Sole Inventions ("Sole Patents") in all countries of the world.

(d) Both Parties shall jointly own any inventions, discoveries, know-how, trade secrets, and other information, that are made jointly by the Parties in the course of the performance of this Agreement ("Joint Inventions"). Subject to subsection (e) below, the RMC shall designate the Party which shall be responsible for filing, prosecuting and maintaining Patents claiming Joint Inventions ("Joint Patents"). All costs and expenses of filing, prosecuting and maintaining such Joint Patents will be borne equally by the Parties. The Party designated by the RMC to perform patenting activities shall seek the comments of the other Party and shall keep the other informed of the progress of such prosecution by providing quarterly status reports and copies of all correspondence between their patent counsel and the patent offices of the countries where such applications were filed. Such other Party shall reasonably assist the Party designated by the RMC in the prosecution of Joint Patents, including, without limitation, by executing any necessary powers of attorney. Subject to the rights and licenses granted to the other Party in Section 2.1(b) and 2.2(b), it is understood that neither Party shall have any obligation to account to the other, or obtain the consent of the owner, with respect to the commercialization, licensing or enforcement of any Joint Patents, and hereby waives any right it may have under the laws of any country to require such accounting or consent.

(e) CG shall have the right but not the obligation (either itself or through its designee) to file, prosecute and maintain Patents claiming Therapeutic Candidates ("Candidate Patents"); provided, however, that for any molecule that is a Therapeutic Candidate and a Target: (i) CG shall have the right but not the obligation (either itself or through its designee) to file, prosecute and maintain Patents claiming uses of such molecule in the CG Program Field and

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such Patents also shall be Candidate Patents; and (ii) Rigel shall have the right, but not the obligation, to file, prosecute and maintain any patents claiming the composition of matter of such molecule or claiming any use of the molecule outside the CG Program Field or in the Rigel Field. All costs and expenses of filing, prosecuting and maintaining Candidate Patents will be

borne by the Party that undertakes such prosecution. The Party undertaking such prosecution shall seek the comments of the other Party and shall keep the other Party informed of the progress of such prosecution by providing quarterly status reports and copies of all correspondence between their patent counsel and the patent offices of the countries where such applications were filed. Each Party shall reasonably assist the other Party in the prosecution of Candidate Patents, including, without limitation, by executing any necessary powers of attorney and other documents necessary for such prosecution.

(f) Each Party agrees to keep the other Party fully informed as to prosecution and maintenance (including without limitation any interference, opposition or other prosecution or other proceedings) with respect to patents claiming and disclosing subject matter within the Program Technology. In the event that a Party elects not to prosecute or maintain any patent rights in a Sole Invention comprising Program Technology, it shall promptly notify the other Party and authorize the other Party to seek or continue such prosecution and maintenance at such other Party's expense. In such case the owner of Sole Invention shall cooperate fully with the other Party to facilitate such prosecution and maintenance.

4.2 INFRINGEMENT AND SIMILAR ACTIONS. As between the Parties hereto:

(a) CG shall have the sole and exclusive right, at its expense, to prosecute any and all infringement or wrongful use of the CG Patents and CG Know-How, and (subject to paragraph (c) below) Sole Patents owned by CG and/or to enter settlements, judgments or other arrangements respecting such infringement or wrongful use. CG may retain all damages and other amounts recovered as a result of any such action, settlement, judgment or other arrangement.

(b) Rigel shall have the sole and exclusive right, at its expense, to prosecute any and all infringement or wrongful use of the Rigel Know-How, the Rigel Biological Materials, and (subject to paragraph (c) below) Sole Patents owned by Rigel and/or to enter settlements, judgments or other arrangements respecting such infringement or wrongful use. Rigel may retain all damages and other amounts recovered as a result of any such action, settlement, judgment or other arrangement.

(c) With respect to infringement of any Program Patents in the CG Program Field, CG shall have the right, but not the obligation (directly or through designees), to institute, prosecute and control at its own expense and for its own benefit, any action or proceeding with respect to such infringement. With respect to infringement of any Program Patents (i.e., outside the CG Program Field), Rigel shall have the right, but not the obligation, (directly or through designees) to institute, prosecute and control, at its own expense and for its own benefit, any action or proceeding with respect to such infringement. If a Party with the right to do so fails to bring an action or proceeding against a suspected infringer within a reasonable period after receiving a written request by the other Party to do so, such other Party shall have the right to

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bring and control an action against such infringer by counsel of its own choice and retain for its own account any amounts recovered from third parties. If one Party brings any such action or proceeding, the other Party agrees to be joined as a Party plaintiff if necessary to prosecute the action and to give the first Party reasonable assistance and authority to file and prosecute the suit.

(d) Each Party shall promptly notify the other in writing of any alleged or threatened infringement of Joint Patents of which it becomes aware and which may adversely impact the rights of the Parties hereunder. Promptly upon such notification, the Parties shall meet to discuss the strategy and appropriate steps to be taken to deal with such infringement. Any recovery obtained by settlement or otherwise shall be disbursed as follows: first, any reasonable expenses incurred in connection with such action (including counsel fees) by both Parties are reimbursed; thereafter, the net recovery shall be shared between the Parties according to the ratio of their respective contributions to the litigation costs. This paragraph shall not be deemed to limit the Parties' respective rights to enforce Joint Patents, or to limit the rights granted under paragraph (c) above.

4.3 THIRD PARTY CLAIMS.

(a) Except to the extent expressly warranted in Article 7, and subject to the indemnification obligation in Article 5, CG shall have no liability to Rigel with respect to any claim, suit or action alleging that the practice of the license rights granted by CG under Section 2.1 infringes

any intellectual property or other right of a third party. Except to the extent expressly warranted in Article 7, and subject to the indemnification obligation in Article 5, Rigel shall have no liability to CG or its Affiliates with respect to any claim, suit or action alleging that the practice of the license rights granted under Section 2.2 infringes any intellectual property or other rights of a third party.

(b) Rigel hereby agrees to provide reasonable assistance to CG, at its request, in defending any action or claim initiated by a third party against CG arising from any claim that the use or practice of the Rigel Know-How, Rigel Biological Materials or the Target by CG or its Affiliates infringes that third party's proprietary rights. CG hereby agrees to provide Rigel reasonable assistance, at its request and expense, in defending any action or claim initiated by a third party against Rigel or its Affiliates arising from any claim that the use or practice of the CG Patents or CG Know-How by Rigel or its Affiliates infringes that third party's proprietary rights.

(c) If a third party asserts against CG that a patent, trademark or other intangible right owned by it is infringed by any product in the CG Program Field derived or resulting from or incorporating Program Technology, CG will be solely responsible for defending against any such assertions at its cost and expense. Each Party will give prompt written notice to the other of any such claim. Rigel will assist in the defense of any such claim as reasonably requested by CG, at CG's expense, and may retain separate counsel at its own expense at any time.

(d) Neither Party shall enter into any settlement of any such claim which would admit the invalidity of Patents within the Program Technology without the other Party's prior written consent, which consent shall not be unreasonably withheld or delayed.

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4.4 PASS-THROUGH ROYALTIES. In consideration for the licenses granted herein:

(a) Rigel agrees to pay any amounts which CG is required to pay to Rockefeller University under the CG License as a result of CG's grant to Rigel of license rights to CG Patents or CG Know-How to Rigel or the exercise of the license rights granted by CG under the CG License.

(b) Rigel agrees to pay CG (i) [*] for the license granted to Rigel hereunder to CG Patents related to the [*] cell lines, and (ii) [*] for each sublicense granted by Rigel under this Agreement.

(c) CG agrees that in the event CG exercises its option to obtain a license pursuant to Section 2.2(a) above, CG will pay any amounts which Rigel is required to pay to Stanford University under the Rigel License as a result of Rigel's grant to CG of license rights to Rigel Biological Material or Rigel Know-How to CG or the exercise of the license rights granted by Rigel under the Rigel License. It is understood that unless and until CG obtains such license rights from Rigel, CG shall not be obligated to pay to Rigel or to Stanford University any amounts that Rigel is required to pay to Stanford University under the Rigel License.

ARTICLE 5

INDEMNIFICATION

5.1 CG INDEMNITY. CG agrees to indemnify, hold harmless and defend Rigel, its Affiliates, agents and employees from and against any and all liabilities, losses, damages, costs, fees and expenses, including reasonable legal expenses and attorneys' fees (collectively, "Losses") arising out of suits, claims, actions, or demands, brought or made by a third party ("Third Party Claim") against Rigel, its Affiliates, agents and employees, based on (i) CG's use and practice of the Rigel Know-How, Rigel Biological Materials, the Program Technology or the Targets, or (ii) breach of CG's warranties under Article 7 below, or (iii) the manufacture, use, handling, storage, sale or other disposition of Rigel Biological Materials, Program Technology, the Targets or any products resulting or derived from the Rigel Biological Materials or the Program Technology by CG, it Affiliates, agents, employees or sublicensees, all except to the extent such Losses or Third Party Claims result from the negligence or willful misconduct of Rigel or a breach of Rigel's warranties under Article 7 below.

5.2 RIGEL INDEMNITY. Rigel agrees to indemnify, hold harmless and defend CG, its Affiliates, agents and employees from and against any and all Losses arising out of any Third Party Claims against CG, its Affiliates, agents and employees based on (i) Rigel's use or practice of the CG Patents the CG Know-How or the Program Technology, (ii) breach of Rigel's warranties under Article 7 below, or (iii) the manufacture, use, handling, storage, sale or other disposition of Program Technology, the Targets or any products resulting or derived from the Program Technology by Rigel, its Affiliates, agents, employees or sublicensees, all except to the extent such Losses or Third Party Claims result from the negligence or willful misconduct of CG, or a breach of CG's warranties under Article 7 below.

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5.3 In the event that a Party is seeking indemnification under this Article 5, it shall inform the other Party of a claim or suit as soon as reasonably practicable after it receives notice of the claim or suit, shall permit the indemnifying Party to assume direction and control of the defense of the claim or suit (including the right to settle the claim or suit solely for monetary consideration), and shall cooperate as reasonably requested (at the expense of the indemnifying Party) in the defense of the claim or suit. Neither Party will enter into any settlement or claim pursuant to this Section 5.3 which is materially adverse to the rights of the other Party herein, without the other Party's prior written consent, which will not be unreasonably withheld or delayed.

ARTICLE 6

CONFIDENTIALITY

6.1 CONFIDENTIALITY. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing, the Parties agree that, for the term of this Agreement and for five (5) years thereafter, the Party receiving any Information or materials furnished to it by the other Party pursuant to this Agreement (collectively, "Confidential Information") shall keep confidential and shall not publish or otherwise disclose or use such Confidential Information for any purpose other than as provided for in this Agreement.

6.2 EXCEPTIONS. The obligations in Section 6.1 shall not apply to any Information or materials to the extent that the receiving Party can establish by competent proof that such Information or materials:

(a) was already known to the receiving Party, other than under an obligation of confidentiality, at the time of disclosure by the other Party;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the receiving Party in breach of this Agreement; or

(d) was disclosed to the receiving Party, other than under an obligation of confidentiality, by a Third Party who had no obligation to the disclosing Party not to disclose such information to others.

6.3 AUTHORIZED DISCLOSURE. Each Party may disclose the other's Confidential Information to the extent such disclosure is reasonably necessary (i) to exercise the rights granted to such Party hereunder (including the right to grant sublicenses as permitted by this Agreement provided that prior to any disclosure to a sublicensee, such sublicensee has executed a confidentiality agreement with terms corresponding to this Article 6); and (ii) to file or prosecute patent applications, to prosecute or defend litigation, to comply with applicable governmental

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regulations or to conduct preclinical or clinical trials; provided that if a Party is required by law or regulation to make any such disclosure of the other Party's Confidential Information it will, except where impracticable for necessary disclosures, for example in the event of medical emergency, give reasonable advance notice to the other Party of such disclosure requirement and, except to the extent inappropriate in the case of patent applications, will use its best efforts to secure confidential treatment of such Confidential Information required to be disclosed.

6.4 SURVIVAL. This Article 6 shall survive the termination or expiration of this Agreement for a period of five (5) years.

ARTICLE 7

WARRANTY MATTERS

7.1 LIMITED WARRANTIES. CG hereby represents and warrants to Rigel that CG has the full right and power to grant the licenses granted to Rigel under Section 2.1(a). Rigel hereby represents and warrants to CG that Rigel has the full right and power to grant the licenses granted to CG under Section 2.2.

7.2 GENERAL WARRANTIES. Each of the Parties hereby represents and warrants to the other that (i) it is a corporation duly organized and validly existing in good standing under the laws of its state of incorporation, (ii) it is duly qualified and authorized to enter into and perform its obligations under this Agreement, (iii) it has full power, authority and legal right to enter into and perform this Agreement, and (iv) the execution, delivery, and performance of this Agreement has been duly authorized by all necessary corporate action on the part of each Party and does not contravene any law binding on it, its Articles of Incorporation or Bylaws, any indenture, mortgage, contract or other agreement to which it is a Party or by which it is bound or any laws, governmental rule, regulation or order.

7.3 INTELLECTUAL PROPERTY WARRANTIES.

(a) Each of the Parties hereby represents and warrants to the other that (i) it does not Control any Patens that would dominate the Patents licensed to the other Party hereunder, (ii) it is not aware of any claims of a third party which would call into question the rights of such Party in the licensed subject matter or its right to grant the licenses granted to the other Party hereunder, (iii) it has provided the other Party with all information concerning royalty obligations pertinent to the licenses granted to the other Party hereunder; and (iv) it will use commercially reasonable efforts to keep in force any license agreement from which the license or sublicense granted to the other Party under this Agreement is derived to the extent that such license agreement does not provide for a survival of any sublicenses granted by such Party.

(b) Rigel further warrants to CG that as of the Effective Date (i) to the best of its knowledge, Rigel's conduct of the Research, and the manufacture, sale and use of Therapeutic Candidates will not infringe any third party intellectual property rights, and without limiting the foregoing, Rigel warrants that Rigel's conduct of the Research will not infringe any of the

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patents listed in Appendix I hereto; (ii) Rigel does not know of any third party other than Stanford University having a claim in the Rigel Biological Materials; and (iii) Rigel has the right to grant to CG a license under the Rigel Biological Materials and the Rigel Know-How to make, use and sell products in the CG [*] Field.

(c) CG further warrants to Rigel that CG has the right to grant to Rigel a license under the CG Patents and CG Know-How to make, use and sell products within the Rigel Field.

(d) Rigel warrants that it has not as of the Effective Date entered into an agreement with any third party licensing or granting rights to Rigel technology in the Field of Research.

7.4 LIMITATION ON WARRANTIES. EXCEPT AS PROVIDED IN SECTIONS 7.1, 7.2, AND 7.3 ABOVE, NEITHER PARTY MAKES ANY WARRANTIES TO THE OTHER PARTY, WHETHER EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE AS TO ANY PRODUCT OR PROCESS, OR AS TO THE VALIDITY OR SCOPE OF ANY PATENTS, OR THAT ANY LICENSED BIOLOGICAL MATERIALS, PATENTS OR KNOW-HOW WILL BE FREE FROM INFRINGEMENT OF

PATENTS OF ANY THIRD PARTY, OR THAT NO THIRD PARTIES ARE INFRINGING SAME.

ARTICLE 8

TERM AND TERMINATION

8.1 TERM OF AGREEMENT. Unless earlier terminated as otherwise provided in this Article 8, this Agreement shall remain in effect until the expiration of the last to expire of the CG Patents or Program Patents.

8.2 TERMINATION FOR BREACH. A Party may terminate this Agreement prior to the expiration of the Agreement in the event that the other Party is in breach of or default under a material term of the Agreement, and the breaching Party does not cure such breach or default within thirty (30) days of written notice thereof from the non-breaching Party. Subject to Section 8.3 below, upon any such termination, all the licensees granted by and between the Parties herein shall terminate; provided that any sublicense granted by a Party hereunder to a third party prior to such termination shall survive such termination, so long as the sublicensee agrees to be bound by the applicable terms of this Agreement.

8.3 SURVIVAL. Upon expiration or termination of this Agreement the rights and obligations under Articles 5 and 6 and Sections 7.4, 8.3, 9.2, 9.3, 9.7 and 9.10 shall continue. In addition, upon expiration or termination of this Agreement after the end of the Research Period, the license granted under Article 2 above and the rights and obligations under Article 4 shall survive. Further, subject to Section 2.1(b) and 2.2(b) if they survive the termination or expiration of this Agreement as provided above, neither Party shall have any obligation to account to the

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other, or obtain the consent of the owner, with respect to the commercialization, licensing or enforcement of any Joint Patents, and hereby waives any right it may have under the laws of any country to require such accounting or consent.

ARTICLE 9

MISCELLANEOUS

9.1 RELATIONSHIP OF THE PARTIES. This Agreement creates only licensor-licensee and sublicensor-sublicensee relationships between Rigel and CG. No partnership or other legal relationship is created hereunder. Neither Party is, or will be deemed to be, an agent or legal representative of the other Party for any purpose. Neither Party will be entitled to enter into any contracts in the name of or on behalf of the other Party, and neither Party will be entitled to pledge the credit of the other Party in any way or hold itself out as having authority to do so.

9.2 ASSIGNMENT. This Agreement may not be assigned by either Party without the prior written consent of the other Party, which consent shall not be unreasonably withheld; provided, however, that a Party may assign this Agreement without such consent to any Affiliate or to a successor in interest by way of merger, acquisition, sale or transfer of substantially all of its business or assets pertaining to the subject matter of this Agreement. The Agreement will be binding upon and inure to the benefit of all permitted successors and assignees of the Parties hereunder, and the name of each Party appearing herein will be deemed to include the names of such Party's successors and assignees.

9.3 USE OF NAMES. No Party hereto may use the name of the other Party in public announcements without the prior consent of the other Party as required by law or regulation.

9.4 AMENDMENT. No amendment, modification or supplement of any provision of the Agreement will be valid or effective unless made in writing and signed by a duly authorized officer of each Party.

9.5 WAIVER. No provision of the Agreement will be waived by any act, omission or knowledge of a Party or its agents or employees except by an instrument in writing expressly waiving such provision and signed by a duly authorized officer of the waiving Party.

9.6 HEADINGS. The headings for each article and section in this Agreement have been inserted for the convenience of reference only and are

not intended to limit or expand on the meaning of the language contained in the particular article or section.

9.7 NOTICES. Any notice or other communication required or permitted to be given to either Party hereto shall be in writing unless otherwise specified and shall be deemed to have been properly given and to be effective on the date of delivery if delivered in person or by facsimile or three (3) days after mailing by registered or certified mail, postage paid, to the other Party at the following address:

If to Rigel: Rigel, Inc.
240 East Grant Avenue
South San Francisco, CA 94080
Attn: Secretary
Fax: 650.624.1101

Copy to: Cooley Godward, LLP
Five Palo Alto Square, 4th Floor
3000 El Camino Real
Palo Alto, CA 94306
Attn: Patrick A. Pohlen, Esq.
Fax: 650.857.0663

If to CG: Cell Genesys, Inc.
342 Lakeside Drive
Foster City, CA 94404
Attn: Chief Executive Officer
Fax: 650.358.0803

9.8 SEVERABILITY. Whenever possible, each provision of the Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of the Agreement is held to be prohibited by or invalid under applicable law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of the Agreement.

9.9 ENTIRE AGREEMENT OF THE PARTIES. The Agreement will constitute and contain the complete, final and exclusive understanding and agreement of the Parties with respect to the subject matter hereof and cancels and supersedes any and all prior negotiations, correspondence, understandings and agreements, whether oral or written, between the Parties respecting the subject matter. Each Party hereto was represented by counsel in drafting and negotiating this Agreement, and all Parties are deemed to have contributed to the drafting hereof.

9.10 GOVERNING LAW. This Agreement shall be governed by and construed in accordance with the laws of the State of California excluding only laws and rules relating to "choice of law". All Parties to this Agreement hereby consent to the jurisdiction of the courts of the State of California and the Federal District Court for the Northern District of California for resolution of any disputes that arise hereunder.

9.11 COUNTERPARTS. This Agreement may be executed in any number of counterparts, each of which shall be an original, but all of which together shall constitute one instrument.

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IN WITNESS WHEREOF, the Parties hereto have duly executed this Agreement as of the date first written above.

CELL GENESYS, INC. RIGEL PHARMACEUTICALS, INC.

By: /s/ Stephen A. Sherwin By: /s/ Donald W. Perryman

Name: Stephen A. Sherwin, M.D.	Name: Donald W. Perryman
Title: Chairman & Chief Executive Officer	Title: VP, Business Development

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APPENDIX A
EXCLUSIVE LICENSE AGREEMENT

EXCLUSIVE LICENSE AGREEMENT made as of January 31, 1996 (the "Effective Date"), by and between Cell Genesys, Inc. ("Company"), a corporation organized and existing under the laws of the State of Delaware, having an office at 322 Lakeside Drive, Foster City, California 94404, and The Rockefeller University ("Rockefeller"), a nonprofit education corporation organized and existing under the laws of the State of New York, having an office at 1230 York Avenue, New York, New York 10021-6395.

WITNESSETH:

WHEREAS, Rockefeller is the owner by assignment from Warren S. Pear, Martin L. Scott, Garry M. Nolan and David Baltimore ("Inventors") of the entire right, title and interest in United States Patent Application Serial No. 08/023,909, filed February 22, 1993, entitled Production of High Titer Helper-Free Retroviruses by Transient Transfection, and in the inventions described and claimed therein ("Licensed Patent Rights"), and in the Biological Materials and related Know-How, as defined below;

WHEREAS, Rockefeller and the Company entered into a license agreement effective as of October 25, 1994 (the "Prior Agreement"), pursuant to which Rockefeller granted to the Company a non-exclusive license to use the Licensed Patent Rights, Know-How and Biological Materials for research and commercial purposes;

WHEREAS, the parties have agreed to expand the scope of the license and rights granted to the Company and therefore have agreed to terminate the Prior Agreement as of the Effective Date, and enter into this Agreement;

WHEREAS, Rockefeller wishes to offer and grant the Company an exclusive license with regard to the Licensed Patent Rights, Know-How and the Biological Materials for research and commercial purposes, and seeks to be compensated for the transfer and use of such rights; and

WHEREAS, the Company wishes to license from Rockefeller the Licensed Patent Rights, Biological Materials and Know-How for commercial development and application as herein defined.

NOW, THEREFORE, in consideration of the mutual benefits to be derived hereunder, the parties hereto agrees as follows:

1. DEFINITIONS.

The following terms will have the meanings assigned to them below when used in this Agreement.

1.1 "AFFILIATE" shall mean:

(a) any entity owning or controlling, directly or indirectly, at least forty-nine percent (49%) of the stock normally entitled to vote for election of directors of a party; or

(b) any entity at least forty-nine percent (49%) of whose stock

normally entitled to vote for election of directors is owned or controlled, directly or indirectly, by a party.

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1.2 "BIOLOGICAL MATERIALS" shall mean (i) the ecotropic producer cell line named [*] which producer cell line was deposited with the American Type Culture Collection as of [*] and has been assigned Accession No. [*] and any viruses produced thereby; (ii) [not disclosed by Cell Genesys] Biological Materials shall also include any direct progeny, mutant, or derivatives of the [*] [not disclosed by Cell Genesys] cell lines and the viruses produced thereby.

1.3 "IMPROVEMENT TECHNOLOGY" means all patent and other intellectual property rights, and materials relating to inventions, discoveries or improvements to the Licensed Technology licensed to Rockefeller by any academic institution, governmental and other not-for-profit entity to which Rockefeller grants a non-exclusive research license with regard to the Licensed Technology pursuant to Section 6.3 herein.

1.4 "KNOW-HOW" shall mean information and data not generally known which are owned and in the possession of or available to Rockefeller and which it is free to divulge as of the Effective Date regarding the preparation and use of Biological Materials, and pharmacological, biological and clinical properties of Biological Materials. It is understood that Know-How shall not include any information or data known by the Company prior to receipt of such information or data from Rockefeller, as shown by reasonable evidence.

1.5 "LICENSED PATENT RIGHTS" shall mean:

(a) the patent application(s) concerning the subject matter of this Agreement which are listed on Exhibit A attached hereto;

(b) all patent applications which are divisions, substitutions, continuations, continuations-in-part, renewals, or additions of the patent applications described in (a) hereof,

(c) all foreign counterparts of the applications listed in (a) and (b) hereof; and

(d) all patents, including reissues, re-examinations and extensions, which may issue on any of the preceding.

1.6 "LICENSED PRODUCTS" shall mean any and all products the manufacture, use or sale of which but for the license granted herein would infringe a Valid Claim or are within the scope of a Pending Claim in the country in which such products are made or sold.

1.7 "LICENSED TECHNOLOGY" shall mean the Licensed Patent Rights, Biological Materials and Know-How.

1.8 "NET SALES" shall mean [*], where [*] shall mean the amount invoiced by the Company or its sublicensees to customers for Licensed Products less: (i) all trade, cash and quantity credits, discounts, refunds or government rebates, (ii) amounts for claims, allowances or credits for returns; retroactive price reductions; chargebacks or the like; (iii) packaging, handling fees and prepaid freight, sales taxes, duties and other governmental charges (including value added tax), but excluding what is commonly known as income taxes; and (iv) provisions for

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uncollectible accounts determined in accordance with reasonable accounting practices, consistently applied to all products of the selling party. [*] shall not include sales by the Company to its Affiliates for resale, provided that if the Company sells a Licensed Product to an Affiliate for resale, [*] shall include the amounts invoiced by such Affiliate to third parties on the resale of such Licensed Product. Notwithstanding the foregoing. [*] shall include charges for the separation, transduction and/or expansion of cells comprising Licensed Products, but notwithstanding any of the foregoing, shall

not include charges for apheresis, reinfusion, surgical procedures, hospital stays or other charges not directly attributed to the Licensed Product or to the ex vivo preparation of the Licensed Product.

1.9 "PARTY" shall mean the Company or Rockefeller, and "Parties" shall mean both the Company and Rockefeller.

1.10 "PENDING CLAIM" shall mean a claim of a pending patent application within the Licensed Patent Rights.

1.11 "TERRITORY" shall mean the entire world.

1.12 "VALID CLAIM" shall mean a claim of an issued and unexpired patent included within the Licensed Patent Rights, which has not been held unenforceable or invalid by a court or other governmental agency of competent jurisdiction, and which has not been admitted to be invalid or unenforceable through reissue, disclaimer or otherwise.

2. LICENSED RIGHTS

2.1 Subject to Section 2.2 below, Rockefeller grants to the Company and its Affiliates the following licenses:

(a) an exclusive, worldwide, royalty-bearing license under the Licensed Technology, with the right to grant and authorize sublicenses, to make, have made, import, have imported, use, sell, offer for sale and otherwise exploit the Licensed Products in any country of the Territory; and

(b) a non-exclusive, worldwide, royalty-free, irrevocable license under the Improvement Technology, with the right to grant and authorize sublicenses, to make, have made, import, have imported, use, sell, offer for sale and otherwise commercialize products and services in any country of the Territory.

2.2 The licenses granted by Rockefeller in Section 2.1 (a) above are subject to any limitations on Rockefeller's rights arising under the provisions of the following:

(a) 35 United States, Section 201 et seq., and regulations and rules promulgated thereunder and any agreements implementing the provisions thereof, or

(b) other applicable laws or regulations to which Rockefeller may be subject; or

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(c) Rockefeller's Institutional Patent Agreement with the United States Department of Health and Human Services, dated June 15, 1973, as amended, which is its formal agreement with the United States Government to implement the cited provisions of the U.S. Code.

2.3 Rockefeller shall promptly notify the Company of any Improvement Technology of which it acquires knowledge and provide the Company all available information relating thereto.

2.4 The licenses herein granted shall continue for the lives of any issued patents hereunder as the same or the effectiveness thereof may be extended by any governmental authority, rule or regulation applicable thereto.

3. TRANSFER OF BIOLOGICAL MATERIALS AND KNOW-HOW

3.1 The parties acknowledge that pursuant to the Prior Agreement, Rockefeller transferred to the Company a quantity of Biological Materials and such Know-How to allow the Company to establish a viable cell culture of said Biological Materials for the Company's purposes. The Company is permitted to cultivate and use said Biological Materials, subject to the terms and conditions of this Agreement. On the Effective Date, Rockefeller shall notify the American Type Culture Collection ("ATCC") that the Company is authorized to receive samples of the Biological Materials deposited with the ATCC and to deliver such materials to the Company at the Company's request, and that the Company has the right to authorize third parties to receive one or more samples of the Biological Materials, on such terms as the Company may indicate to the ATCC.

3.2 Should the Company exhaust the quantity of Biological Materials within six (6) months of the date of execution hereof, so that a viable cell culture of said Biological Materials no longer exists, Rockefeller shall

authorize the ATCC to provide the Company with a quantity of Biological Materials sufficient to reestablish the Company's viable colony thereof.

3.3 Within sixty (60) days of the Effective Date, Rockefeller shall deliver to the Company tangible copies of all existing Know-How which it did not previously provide to the Company pursuant to the Prior Agreement.

4. PAYMENTS

4.1 In consideration of the rights and licenses granted hereunder, the Company shall pay or cause to be paid to Rockefeller amounts as follows:

(a) [Not disclosed by Cell Genesys]

(b) [Not disclosed by Cell Genesys]

(c) [Not disclosed by Cell Genesys]

(d) a royalty of [*] of Net Sales of Licensed Products sold by the Company within the scope of a Valid Claim within the Licensed Patent Rights in the country they are made or sold.

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Notwithstanding the above, the royalty due Rockefeller on Net Sales of Licensed Products, the manufacture, use or sale of which would not infringe a Valid Claim in the country for which they are sold but which are within the scope of a Pending Claim in such country, shall be fifty percent (50%) of the royalty due under Section 4.1(d).

4.2 In the event that a Licensed Product is sold in combination as a single product with another product whose sale and use are not covered by the Licensed Patent Rights in the country for which the combination product is sold, Net Sales from such sales, for purposes of calculating the amounts due under Section 4.1 above, shall be calculated by multiplying the Net Sales of that combination by the fraction A/(A + B), where A is the gross selling price of the Licensed Product, as the case may be, sold separately, and B is the gross selling price of the other product sold separately. In the event that no such separate sales are made by the Company, Net Sales for royalty determination shall be as reasonably allocated by the Company between such Licensed Product and such other product, based upon their relative importance and proprietary protection.

4.3 Licensed Products sold, leased or otherwise distributed by the Company's sublicensees shall be considered to be sales, leases or disposals of Licensed Products by the Company for purposes of royalty payments and reports under this Agreement. The obligation to pay royalties pursuant to this Agreement is imposed only once with respect to the sale of a particular Licensed Product regardless of the number of claims or patents that cover such Licensed Product. The Company shall have no obligation to pay royalties on Licensed Products used in research and development, in clinical trials or other noncommercial purposes, or distributed as samples.

4.4 The Company's obligation to pay royalties hereunder shall continue on a country-by-country basis until (i) the expiration of the last-to-expire issued patent within the Licensed Patent Rights in such country, or (ii) [*] following the first commercial sale of a Licensed Product in a country, if no patent covering such Licensed Product has been issued in such country. Thereafter, the Company shall have a fully paid up license under Licensed Patent Rights, Biological Materials and Know-How to make, have made, use, sell, lease, import, have imported, offer for sale or otherwise exploit the Licensed Product(s) for any use in that country.

4.5 [Not disclosed by Cell Genesys]

4.6 [Not disclosed by Cell Genesys]

4.7 Unless this Agreement is terminated earlier, within sixty (60) days following the first achievement by the Company or a sublicensee of the following milestones with respect to the first Licensed Product within the scope of a Valid Claim within the Licensed Patent Rights, the Company shall pay to Rockefeller [*] milestone payments as follows:

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<TABLE>
<CAPTION>

EVENT	Payment
<S>	<C>
Enrollment of first patient in a Company-sponsored [*] clinical trial of a Licensed Product	$ [*]
Enrollment of first patient in a Company-sponsored [*] clinical trial of a Licensed Product	$ [*]
Approval of NDA in U.S. of a Licensed Product	$ [*]

</TABLE>

4.8 Upon commencement of commercial sales of any Licensed Products which generate a royalty to Rockefeller pursuant to this Agreement, the Company shall within ninety (90) days of the close of the fiscal semi-annual period, provide semi-annual reports to Rockefeller showing the total Net Sales of Licensed Products sold, leased or otherwise disposed of during such period and the calculation of royalties thereon. Any royalty then due and payable shall be included with such report. All reports provided hereunder by the Company shall be the Confidential Information of the Company, subject to Section 7 herein. The Company's records shall be open to inspection by an independent certified public accountant designated by Rockefeller for three (3) years from the submission of such reports and payments, subject to execution of a confidentiality agreement reasonably acceptable to the Company, once per calendar year at reasonable times, at Rockefeller's expense, for the sole purpose of verifying the accuracy of the reports and royalty payments made by the Company. The accountant shall report to Rockefeller only whether there has been an underpayment and, if so, the amount thereof.

5. TIMES AND CURRENCIES OF PAYMENT

5.1 Royalty payments shall be made in United States dollars or if sales are made in the currency of other countries, royalties shall be calculated in the currency of such other country and be converted into United States dollars using the applicable exchange rate for sale of U.S. dollars listed by the foreign exchange desk of the Bank of America on the last day of the applicable reporting period.

5.2 If at any time legal restrictions prevent the prompt remittance of part or all royalties by the Company with respect to any country where a Licensed Product is sold, the Company shall have the right and option to make such payment by depositing the amount thereof in local currency to an account in the name of Rockefeller in a bank or other depository in such country.

6. SUBLICENSEES

6.1 The Company and its Affiliates shall have the right to grant and authorize sublicenses under the Licensed Technology and Improvement Technology to commercial entities for research purposes and for commercial purposes, including without limitation, to make, have made, import, have imported, use, lease, offer for sale and sell Licensed Products in the Territory.

6.2 The Company shall have the sole discretion to determine the financial and other terms on which any sublicenses shall be granted under the Licensed Technology, subject to the

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provisions herein. Any sublicense(s) granted by the Company under this Agreement shall be subject and subordinate to the terms and conditions of this Agreement, except the financial terms of the sublicense(s) may require greater payments than the financial terms in this Agreement.

6.3 Notwithstanding Section 2.1 above, Rockefeller, on behalf of the Company, may continue to grant limited, non-transferable, research sublicenses to academic institutions, governmental and other not-for-profit entities using the form sublicense agreement attached hereto as Exhibit B. Rockefeller shall not enter into or agree to enter into any agreement with such an entity which deviates in any way from the form agreement set forth in Exhibit B, without the prior written consent of the Company. Rockefeller

shall provide the Company with a copy of each such research license entered by Rockefeller promptly following the execution of such agreement.

6.4 In the event of any termination of this Agreement, any sublicenses granted under or this Agreement shall also terminate unless such sublicensees provide Rockefeller written notice that they will abide by the applicable terms of this Agreement.

6.5 In no event shall a default or breach of a sublicensee of a sublicense granted by the Company pursuant to this Agreement constitute by a default or breach by the Company of this Agreement or be deemed a valid basis for the termination of this Agreement.

7. CONFIDENTIAL INFORMATION

7.1 Each Party and its Affiliates and sublicensees shall treat as confidential all Confidential Information received from the other Party hereto, shall not use such Confidential Information except as expressly set forth herein or otherwise authorized in writing, shall implement reasonable procedures to prohibit the disclosure, unauthorized duplication, misuse or removal of such Confidential Information and shall not disclose such Confidential Information to any third party except as may be necessary and required in connection with the rights and obligations of such party under this Agreement, and subject to confidentiality obligations at least as protective as those set forth herein. Without limiting the foregoing, each of the parties shall use at least the same procedures and degree of care which it uses to prevent the disclosure of its own confidential information to prevent the disclosure of Confidential Information of the other Party. As used herein, the term "Confidential Information" shall mean any information expressly designated as Confidential Information in this Agreement and information disclosed by one Party to another pursuant to this Agreement which is in written, graphic, machine readable or other tangible form and is marked "Confidential" to indicate its confidential nature. Confidential Information may also include oral information disclosed by one Party to another pursuant to this Agreement, provided that such information is designated as confidential at the time of disclosure and within thirty (30) days after its oral disclosure is reduced to a written summary by the disclosing Party, which summary is marked in a manner to indicate its confidential nature and delivered to the receiving Party.

7.2 Notwithstanding the above, neither Party has any obligation of confidence under this Agreement with respect to any information which:

(i) may be demonstrated to have been known to the receiving Party prior to the time of disclosure thereof by the disclosing Party; or

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(ii) without breach of this Agreement, has been published or is otherwise available to the public at any time whether before or after the time of disclosure to such Party; or

(iii) is at any time lawfully received by such Party from a third party who has no obligation of confidence to a Party in respect hereof.

7.3 Each Party hereto may disclose another's Confidential Information to the extent such disclosure is reasonably necessary in filing or prosecuting patent applications, prosecuting or defending litigation, complying with applicable governmental regulations or otherwise submitting information to tax or other government authorities, making a permitted sublicense or other exercise of its rights hereunder or conducting clinical trials, provided that if a Party is required to make any such disclosure of another Party's secret or Confidential Information, other than pursuant to a confidentiality agreement, it will give reasonable advance notice to the latter Party of such disclosure requirement and, will use its best efforts to secure confidential treatment of such information prior to its disclosure (whether through protective orders or otherwise).

8. REPRESENTATIONS AND WARRANTIES

8.1 Rockefeller represents and warrants that: (i) it is a nonprofit corporation duly organized, validly existing and in good standing under the laws of New York; (ii) the execution, delivery and performance of this Agreement have been duly authorized by all necessary action on the part of Rockefeller; (iii) it is the sole and exclusive owner of all right, title and interest in the Licensed Patent Rights; (iv) the Licensed Patent Rights are free and clear of any lien, security interest or restriction on transfer or license; (v) Rockefeller has not previously granted, and will not grant

during the term of this Agreement, any right, license or interest in and to the Licensed Patent Rights, Biological Materials and Know-How, or any portion thereof, in conflict with the rights, exclusive license and interest granted to the Company herein; (vi) it has complied fully with all requirements of 35 U.S.C. Section 201 et seq. and all implementing regulations with respect to perfecting its interest in the Licensed Patent Rights; (vii) Exhibit A contains a complete and accurate listing of all Licensed Patent Rights existing as of the Effective Date; and (viii) there are no actions, suits, investigations, claims or proceedings pending in any way relating to the Licensed Patent Rights, Biological Materials or Know-How.

8.2 The Company represents and warrants that: (i) it is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware; and (ii) the execution, delivery and performance of this Agreement have been duly authorized by all necessary corporate action on the part of the Company.

8.3 ROCKEFELLER EXPRESSLY DISCLAIMS ANY AND ALL IMPLIED OR EXPRESS WARRANTIES AND MAKES NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE OF BIOLOGICAL MATERIALS, LICENSED PROCESSES OR LICENSED PRODUCTS CONTEMPLATED BY THIS AGREEMENT. FURTHER, ROCKEFELLER HAS MADE NO FORMAL INVESTIGATION AND THEREORE CAN MAKE NO REPRESENTATION THAT BIOLOGICAL MATERIALS SUPPLIED BY IT OR THE METHODS USED IN MAKING OR

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USING SUCH MATERIALS ARE NOW OR WILL REMAIN FREE FROM LIABILITY FOR PATENT INFRINGEMENT.

9. [Not disclosed by Cell Genesys]

9.1 [Not disclosed by Cell Genesys]

9.2 [Not disclosed by Cell Genesys]

10. PUBLICITY

The Company will not use either directly or by implication the name of Rockefeller, or the name of any member of the faculty or staff thereof for any commercial or promotional purposes without prior notification and written agreement of Rockefeller. Except as expressly provided herein, the Parties agree not to disclose the terms of this Agreement to any third party without the prior written consent of the other Party to the fact and form of such disclosure, except as required by securities or other applicable laws, to prospective investors and to such party's accountants, attorneys and other professional advisors. Notwithstanding the above, the Company may disclose the existence of this Agreement and issue a press release, reasonably acceptable to Rockefeller, describing this Agreement and the rights granted the Company by Rockefeller under this Agreement, and disclose to actual and potential sublicensees the rights granted the Company by Rockefeller under this Agreement.

11. PATENTS

11.1 Except as set forth in Section 11.4, the Company shall have the sole right to control the preparation, filing, prosecution and maintenance of the Licensed Patent Rights, and any interference or opposition proceeding relating thereto, using patent counsel of its choice. The Company shall consult with Rockefeller regarding the prosecution of any such patent applications, by providing Rockefeller a reasonable opportunity to review and comment on all proposed submissions to any patent office before submittal, and provided further that the Company shall keep Rockefeller reasonably informed as to the status of such patent applications by promptly providing Rockefeller copies of all communications relating to such patent applications that are received from any patent office. If the Company informs Rockefeller in writing that the Company no longer wishes to conduct such activities with regard to any such patent applications or patents in any country, then Rockefeller will be free, at its discretion and expense to either abandon the subject patent applications or to continue such activities, and the Company shall have no further rights with respect to the applicable patent applications or patents in such countries.

11.2 During the term of the Agreement, the Company shall be responsible for one hundred percent (100%) of the expenses incurred in connection with the activities set forth in Section 11.1. above. [Not disclosed by Cell Genesys] With respect to patent-related costs incurred after the Effective Date, the Company shall reimburse Rockefeller within thirty (30) days

following invoice for such costs, in a form reasonably acceptable to the Company.

11.3 If either Party hereto becomes aware that any Licensed Patent Rights are being or have been infringed by any third party, such Party shall promptly notify the other Party hereto in

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writing describing the facts relating thereto in reasonable detail. The Company shall have the initial right, but not the obligation, to institute, prosecute and control any action, suit or proceeding (an "Action") with respect to such infringement, including any declaratory judgment action, at its expense, using counsel of its choice; provided, however, during the pendency of any such Action, the Company shall be entitled to place any royalties otherwise due Rockefeller hereunder in a separate account controlled by the Company. If the pertinent Licensed Patent Rights are found invalid or unenforceable in such an Action, or any appeal thereof, the Company may retain the amounts placed in such account without further obligation to Rockefeller with regard thereto. If the Licensed Patent Rights are not held invalid or unenforceable in such an Action, or any appeal thereof, the Company shall promptly pay the amounts deposited in such account to Rockefeller. Any amounts recovered from third parties in any such Action shall be retained by the Company. In the event the Company fails to initiate or defend any Action involving the Licensed Patent Rights within one (1) year of receiving notice of any commercially significant infringement, Rockefeller shall have the right, but not the obligation, to initiate and control such an Action, and the Company shall cooperate reasonably with Rockefeller, at Rockefeller's request, in connection with any such Action. Any amounts recovered in such Action shall be used first to reimburse the Company and Rockefeller for the expenses incurred in connection with such Action, and any remainder retained by Rockefeller.

11.4 In the event the parties believe an interference may be declared or an interference is declared between any patent application or patent within the Licensed Patent Rights and any patent application or patent owned or controlled by the Company relating to the production of high titer retroviruses, the parties agree to amicably settle any such prospective or actual interference in accordance with the procedure set forth on Exhibit C. The Company shall have the exclusive right to initiate such settlement procedure after consultation with Rockefeller. In the event of any such prospective or actual interference and the settlement thereof, each Party shall pay its own costs associated therewith and the parties shall equally share the costs of any arbitration, including without limitation, administration and arbitrator fees. It is understood and agreed that in the event an interference is declared, neither Patty shall have an obligation to participate in such a proceeding, but each hereby acknowledges that it understands that a failure to participate may result in an adverse outcome which could have a material adverse impact on such Party. It is further understood and agreed that any patent applications and patents within the Licensed Patent Rights which are involved in any interference shall remain subject to the license granted the Company herein.

12. LICENSED PRODUCT LIABILITY

The Company agrees to indemnify, defend and hold harmless Rockefeller and its trustees, officers, agents, faculty, employees, and students (the "Indemnitees"), from any and all liability arising from injury or damage to persons or property resulting directly or indirectly from the Company's acquisition, use, manufacture, sublicense or sale of any Licensed Product covered by Licensed Patent Rights or Know-How licensed hereunder. Notwithstanding the foregoing, the Company expressly retains any and all claims it may have against Indemnitees arising from Indemnitees' negligence or willful misconduct. The Company's obligation to indemnify the Indemnitees under this Section 11 shall not apply unless the indemnified Party promptly notifies the Company of any claim or liability subject to this Section 12 and cooperates fully with the Company in the defense of any such claim or proceeding. The Company further agrees to obtain, prior to the first

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commercial sale of a Licensed Product, and maintain in force for at least fifteen (15) years following the last sale of a Licensed Product, product liability insurance coverage of at least one million ($1,000,000) dollars or a lesser amount as appropriate to the risk as determined by reference to reliable standards in the industry, such insurance to specifically name Rockefeller as an additional insured.

13. NOTICES

Any notice required to be given pursuant to this Agreement shall be in writing and may be made by personal delivery or by registered or certified mail, return receipt requested, by one Party to the other Party at the addresses noted below:

In the case of the Company, notice should be sent to:

Cell Genesys, Inc.
322 Lakeside Drive
Foster City, California 94404
Attn: Senior Vice President, Corporate Development

In the case of Rockefeller, notice should be sent to:

The Rockefeller University
1230 York Avenue
New York, New York 10021
Attn: Office of the General Counsel

14. LAW TO GOVERN

This Agreement shall be interpreted and governed in accordance with the laws of the State of New York.

15. ASSIGNMENT

This Agreement may not be assigned by either Party without the prior written consent of the other; PROVIDED, HOWEVER, the Company may assign this Agreement in connection with the transfer of all or substantially all of its business relating to the subject matter of this Agreement whether by sale, merger, operation of law or otherwise.

16. TERMINATION

16.1 The Company shall have the right to terminate this Agreement at any time with respect to any Licensed Patent Right or any country upon ninety (90) days prior written notice to Rockefeller. Such termination shall automatically terminate the license rights provided in Section 2 with respect to such Licensed Patent Rights hereof in such country but shall not relieve the Company of the obligation to pay royalties for any period prior to the effective date of termination.

16.2 Either Party may terminate this Agreement in the event of a material breach by the other Party which is not cured within a reasonable time, provided only that the offending Party is given notice of the breach and not less than ninety (90) days in which to cure such breach.

16.3 Sections 2.4, 6.4 and 24.3 and Articles 7, 8, 10, 12, 14, 17 and 25 shall survive expiration or termination of this Agreement for any reason.

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17. RESOLUTION OF DISPUTES

The Parties agree that in the event of it dispute between them arising from, concerning, or in any way relating to this Agreement, the Parties shall undertake good faith efforts to resolve the same amicably between themselves.

18. FORCE MAJEURE

The Parties shall not be liable in any manner for failure or delay in fulfillment of all or part of this Agreement, directly or indirectly caused by acts of God, governmental orders or restrictions, war, war-like conditions, revolution, riot, looting, strike, lockout, fire, earthquake, flood or other similar or dissimilar cause or circumstances beyond the nonperforming Party's control. The nonperforming Party shall promptly notify the other Party of the cause or circumstance and shall recommence its performance of its obligations as soon as practicable after the cause or circumstance ceases.

19. BINDING UPON SUCCESSORS AND ASSIGNS

Subject to the limitations on assignment herein, this Agreement shall be binding upon and inure to the benefit of successors in interest or assigns of Rockefeller and the Company. Any such successor or assignee of a Party's interest shall expressly assume in writing the performance of all the terms and conditions of this Agreement to be performed by said Party.

20. INDEPENDENT CONTRACTORS

The relationship between Rockefeller and the Company is that of independent contractors. Rockefeller and the Company are not joint venturers, partners, principal and agent, master and servant, employer or employee, and have no other relationship other than independent contracting parties. Rockefeller shall have no power to bind or obligate the Company in any manner, other than as is expressly set forth in this Agreement. Likewise, the Company shall have no power to bind or obligate Rockefeller in any manner, other than as is expressly set forth in this Agreement.

21. SEVERABILITY

If any provision of this Agreement is ultimately held to be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not in any way be affected or impaired thereby.

22. NO WAIVER

Any delay in enforcing a Party's rights under this Agreement or any waiver as to a particular default or other matter shall not constitute a waiver of such Party's rights to the future enforcement of its rights under this Agreement, excepting only as to an express written and signed waiver as to a particular matter for a particular period of time.

23. NO IMPLIED OBLIGATIONS

It is understood and agreed that nothing in this Agreement shall be deemed to prevent the Company from commercializing technology or products similar to or competitive with the Licensed Technology or the Licensed Products. Nor shall anything in this Agreement impair the

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right of the Company to independently acquire, license, develop or have others develop for it technology performing similar or equivalent functions as the Licensed Technology, or to develop, market or distribute products based on such technology in addition to or in lieu of the Licensed Products.

24. COMPLIANCE WITH LAWS. REGULATIONS AND STANDARDS

24.1 The Company recognizes that the use of Biological Materials carries with it certain safety risks to both the environment and the population that are inherent in such materials, and shall exercise prudent scientific laboratory procedures in the use of said Biological Materials.

24.2 The inventors and Rockefeller recognize and have advised that the Biological Materials may be used to create infectious retroviruses with a broad host range, that the supplied materials may be used to create retroviruses that can infect human cells in both vitro and in vivo, that the Biological Materials and all materials derived thereof should be handled and used with all due care in accordance with generally acceptable scientific guidelines establishing appropriate precautions and approved by the Institutional Biosafety Committee or similar authority at the Company.

24.3 The Company shall bear all risk to the Company and/or to any others resulting from use, directly or indirectly, to which the Company puts the Biological Materials or any progeny or cells or cell lines derived from it.

25. NO CONSEQUENTIAL DAMAGES

IN NO EVENT SHALL EITHER PARTY BE LIABLE FOR SPECIAL, INCIDENTAL OR CONSEQUENTIAL DAMAGES ARISING OUT OF ANY BREACH OF THIS AGREEMENT.

26. ENTIRE UNDERSTANDING

This Agreement with its Exhibits represents the entire understanding between the Parties with respect to the subject matter hereof and supersedes any other agreement, expressed or implied, by the Parties with respect to the Licensed

Patent Rights, Biological Materials, Know-How and Improvement Technology, and supersedes and merges all prior negotiations, discussions and agreements, including without limitation, the Prior Agreement between the parties. This Agreement may not be amended or modified except in a written document signed by authorized representatives of the Parties.

IN WITNESS WHEREOF, the Parties have caused this Agreement to be duly executed as of the day and year first above written.

CELL GENESYS, INC.

By: /s/ R. Scott Greer

Title: Senior Vice President
Corporate Development

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Date: February 2, 1996

The Rockefeller University

By: /s/ William H. Griesar

Title: Vice President and General Counsel

Date: January 31, 1996

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EXHIBIT "A"

LICENSED PATENT RIGHTS

United States Serial No. 08/023,909

PCT Application No. PCT/US94/01983

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AMENDMENT TO EXCLUSIVE LICENSE AGREEMENT

This Amendment to Exclusive License Agreement ("Amendment"), effective as of November 3, 1998, by and between Cell Genesys, Inc.,("Company"), a corporation organized and existing under the laws of the State of Delaware, having an office at 342 Lakeside Drive, Foster City, California 94404, and The Rockefeller University ("Rockefeller"), a nonprofit education corporation organized and existing under the laws of the State of New York, having an office at 1230 York Avenue, New York, New York 10021-6395 (Company and Rockefeller collectively, the "Parties").

BACKGROUND

The Parties desire to amend that certain Exclusive License Agreement by and between Company and Rockefeller effective as of January 31, 1996 (the "Agreement") as set forth herein below.

NOW, THEREFORE, the Parties agree as follows:

1. AMENDMENT. This Amendment hereby amends the Agreement to incorporate the terms and conditions set forth in this Amendment. The relationship of the Parties shall continue to be governed by the terms and conditions of the Agreement, as amended herein; and in the event that there is any conflict between the terms and conditions of the Agreement and this Amendment, the terms and conditions of this Amendment shall control. As used in this Amendment, all capitalized terms shall have the meanings defined for such terms in this Amendment or, if not defined in the Amendment, the meanings defined in the Agreement.

2. MODIFICATION TO THE AGREEMENT.

2.1 Section 4.6 of the Agreement is hereby amended to read in its entirety as follows:

"4.6 COMMERCIAL SUBLICENSES. It is understood and agreed that Company shall have the right, at its sole discretion, to grant Commercial Sublicenses to third parties [not disclosed by Cell Genesys]. As used herein, "Commercial Sublicense" shall mean Commercial Target Sublicenses and any other sublicense right granted under the Licensed Technology; provided, however, Commercial Sublicenses shall exclude rights granted by Company to a third party pursuant to an agreement substantially in the form of Exhibit D to this Agreement (i.e., research sublicenses)."

2.2 The Agreement is hereby amended to add the following new Section 4.9:

"4.9 COMMERCIAL TARGET SUBLICENSES. Subject to the terms and conditions set forth in this Section 4.9 below and without limiting the provisions of Section 4.6 above or Article 6 below, Company shall have the right to grant and authorize Commercial Target Sublicenses to third parties (each such third party, a "Commercial Target Sublicensee") on terms and conditions as Company deems appropriate in its sole discretion.

(a) MILESTONE AND MAINTENANCE FEES. In addition to amounts payable

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pursuant to Section 4.3 above and in consideration of Company's

right to grant and authorize Commercial Target Sublicenses pursuant to this Section 4.9 [not disclosed by Cell Genesys]. Payments due under this Section 4.9(a) shall be due and payable within sixty (60) days after the calendar quarter in which the Milestone Fee or Maintenance Fee, as applicable, is received by Company [not disclosed by Cell Genesys].

(b) TERMS. For purposes of this Section 4.9 the following capitalized terms shall have the following meanings. "Commercial Target Sublicense" shall mean a sublicense under the Licensed Technology that includes the right to conduct Target Validation using the Licensed Technology. "Target Validation" shall mean the process by which the function of nucleotide sequences are identified, determined and/or confirmed; and/or the function of nucleotide sequences are identified, determined and/or confirmed as being significant in a disease or other biological pathway in which pharmacological or other intervention is sought to affect the function of that pathway.
[Not disclosed by Cell Genesys].

(c) SURVIVAL. Subject to Section 6.4 below, Commercial Sublicenses, including Commercial Target Sublicenses, shall survive the termination of this Agreement, provided that the Commercial Sublicensee or Commercial Target Sublicensee, as the case may be, agrees to be bound by the applicable terms and conditions of this Agreement."

3. ENTIRE AGREEMENT. Together the Agreement (including the Exhibits thereto) and this Amendment constitute the entire agreement between the Parties in connection with the subject matter thereof and supersede all prior and contemporaneous agreements, understandings, negotiations and discussions, whether oral or written, of the Parties.

IN WITNESS WHEREOF, the Parties have executed this Amendment.

CELL GENESYS, INC.	The Rockefeller University
By: /s/ Bruce A. Hironaka	By: /s/ William A. Griesar
Title: Vice President, Corp. Devel.	Title: Vice President and General Counsel
Date: November 16, 1998	Date: 11/3/98

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APPENDIX B

BOSC 23 CELL LINE

CGI Docket Number	Application, Patent Number or Publication Number	Filling Date, Grant Date, or Publication Date	Title/Inventors
The Rockefeller University	PCTWO94/19478 (US application corresponding to the PCT)		Production of High Titer Helper-Free Retroviruses by Transient Transfection Pear at al.
The Rockfeller University Transfection	US 08/693,160	June 12, 1996	Production of High Titer Helper-free Retroviruses by Transient Pear, at al.

KAT-TM

CELL 13.0 Virus & Mediated	US 5,834,256 (Patent)	November 10, 1998	Method for Production of High Titer High Efficiency of Retroviral Transduction of Mammalian Cells Finer at al.
CELL 13.1 Virus & Mediated	US 5,686,279 (Patent)	November 11, 1997	Method for Production of High Titer High Efficiency of Retroviral Transduction of Mammalian Cells Finer at al.
CELL 13.1 PCT Virus & Mediated	WO 94/29438	December 22, 1994	Method for Production of High Titer High Efficiency of Retroviral Transduction of Mammalian Cells Finer at al.
CELL 13.2 Virus & Mediated	US 5,858,740 (Patent)	January 12, 1999	Method for Production of High Titer High Efficiency of Retroviral Transduction of Mammalian Cells Finer at al.
CELL 13.3 Virus & Mediated	US 08/517,488	August 21, 1995	Method for Production of High Titer High Efficiency of Retroviral Transduction of Mammalian Cells Finer at al.

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KAT-TM-

CGI Docket Number	Application, Patent Number or Publication Number	Filling Date, Grant Date, or Publication Date	Title/Inventors
CELL 13.3 PCT Virus & Mediated	WO 97/07225	February 21, 1997	Method for Production of High Titer High Efficiency of Retroviral Transduction of Mammalian Cells Finer at al.
CELL 13.5 Virus & (will be dropped if Mediated 13.3 is allowed)	US 09/266,956	March 11, 1999	Method for Production of High Titer High Efficiency of Retroviral Transduction of Mammalian Cells Finer at al.
	US 08/914,893	August 20, 1997	Method for Production of High Titer Virus & High Efficiency of Retroviral Mediated Transduction of Mammalian Cells Finer at al.

APPENDIX C

RIGEL BIOLOGICAL MATERIALS

[*] Vectors:

[*]

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APPENDIX D

NOLAN AND NOLAN/ROTHENBERG PATENTS

U.S. Patent Application No. 08/589,109, entitled "Methods for Screening for Transdominant Effector Peptides and RNA Molecules" (the Nolan/Rothenberg Patent Application).

U.S. Patent Applications Nos. 08/789,333, 08/589,911 and 08/963,368, entitled, "Methods for Screening for Transdominant Intracellular Effector Peptides and RNA Molecules" (the Nolan Patent Application).

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APPENDIX E

LICENSE AGREEMENT

BY AND BETWEEN

THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY

AND

RIGEL PHARMACEUTICALS, INC.

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APPENDIX E

LICENSE AGREEMENT

Effective as of June 1, 1999 (the "Effective Date"), THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY, a body having corporate powers under the laws of the State of California ("STANFORD") and RIGEL PHARMACEUTICALS, INC., a Delaware corporation having a principle place of business at 240 East Grand Avenue, South San Francisco, CA 94080 ("RIGEL"), agree as follows:

RECITALS

A. STANFORD owns certain [*] cell lines and derivatives thereof and biological components related thereto.

B. RIGEL desires to obtain a non-exclusive license to such materials for use in the Field, with the right to grant one non-exclusive sublicense to Cell Genesys, Inc.

1. DEFINITIONS.

1.1 "CELL GENESYS" means Cell Genesys, Inc., a Delaware corporation, having a principal place of business at 342 Lakeside Drive, Foster City, CA 94404.

1.2 "FIELD" means any and all fields of use, including, without limitation, any research or commercial field of use.

1.3 "LICENSED BIOLOGICAL MATERIALS" means the materials listed on Exhibit A.

1.4 "LICENSED KNOW-HOW" means:

(a) any and all tangible or intangible know-how, trade secrets, inventions (whether or not patentable), processes, data, and other information owned by STANFORD as of the Effective Date that are necessary or useful for the use of the Licensed Biological Materials; and

(b) any modifications or progeny of the information and materials in subsection (a) above that STANFORD may elect to provide to RIGEL at STANFORD's sole and exclusive discretion.

1.5 "PATENT" shall mean all foreign and domestic patents (including, without limitation, extensions, reexaminations, reissues, renewals and inventors certificates) and patents issuing from patent applications (including substitutions, provisionals, divisionals, continuations and continuations-in-part).

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2. GRANT; TRANSFER OF LICENSED BIOLOGICAL MATERIALS.

2.1 STANFORD hereby grants, and RIGEL hereby accepts, a worldwide, non-exclusive license (without the right to sublicense except to Cell Genesys in the field of human and/or animal gene therapy as provided in Article 8) under STANFORD's right, title and interest in the Licensed Biological Materials to conduct research and development and to use the Licensed Biological Materials to make, have made, use, import, offer for sale and sell products in the Field.

2.2 STANFORD hereby grants, and RIGEL hereby accepts, a worldwide, non-exclusive license (without the right to sublicense except to Cell Genesys in the field of human and/or animal gene therapy as provided in Article 8) under STANFORD's right, title and interest in the Licensed Know-How to use the Licensed Know-How in the Field.

2.3 STANFORD shall have the right to use the Licensed Know-How and the Licensed Biological Materials for its own bona fide research, including sponsored research and collaborations. In addition, STANFORD shall have the right to distribute the Licensed Biological Materials.

2.4 Promptly after the Effective Date, STANFORD shall transfer to RIGEL such quantities of the Licensed Biological Materials as RIGEL shall reasonably request. Thereafter, STANFORD shall transfer to RIGEL such additional quantities of Licensed Biological Materials as RIGEL shall reasonably request in the event that RIGEL's stock of the Licensed Biological Materials is destroyed or contaminated.

3. LICENSE ROYALTIES.

3.1 In partial consideration for the license granted by STANFORD to RIGEL under Section 2.1, RIGEL agrees to pay to STANFORD the following:

(a) An initial, nonrefundable license issue royalty of [*], which amount shall be paid within thirty (30) days after the Effective Date.

(b) A royalty payment equal to [*] on each of the first three (3) anniversaries of the Effective Date.

After the third (3rd) anniversary of the Effective Date, the sublicense shall be considered perpetual and fully paid-up.

3.2 If RIGEL grants to Cell Genesys a sublicense under the Licensed Biological Materials to use and sell products in the field of human and/or animal gene therapy, RIGEL shall pay to STANFORD during the term of such sublicense a sublicense fee as follows:

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Upon signing of the sublicense	$[*]
On each of the first three (3) anniversaries of the effective date of such sublicense	$[*]
On the 4th, 5th and 6th anniversaries of the effective date of such sublicense	$[*]

After the sixth (6th) anniversary of the effective date of such sublicense, the sublicense shall be considered perpetual and fully paid-up.

4. PATENTS; NEW INVENTIONS.

Subject to the terms and conditions of this Agreement, any patentable inventions or discoveries conceived or reduced to practice by the employees, agents or consultants of one party during the course of the Agreement ("Sole Inventions") shall be the property of such party. Any patentable inventions or discoveries conceived or reduced to practice jointly by employees, agents or consultants of STANFORD and RIGEL as determined in accordance with United States rules of inventorship ("Joint Inventions") during the course of and pursuant to this Agreement shall be owned jointly by STANFORD and RIGEL, each to own an undivided one-half (1/2) interest in such Joint Invention. Each party shall cooperate with the other in completing any patent applications relating to Joint Inventions, and in executing and delivering any instrument required to assign, convey or transfer to such other party its undivided one-half (1/2) interest.

5. WARRANTIES.

5.1 STANFORD's Office of Technology Licensing represents and warrants that to the best of its knowledge as of the Effective Date, STANFORD has not sought or obtained patent protection of the Licensed Biological Materials or any use thereof in the Field.

5.2 STANFORD's Office of Technology Licensing represents and warrants that as of the Effective Date, it has no knowledge of claims by third parties that the use of the Licensed Biological Materials infringes any patents, copyrights or other rights of third parties.

5.3 STANFORD represents and warrants that it has all right, power and authority necessary to grant the licenses set forth in Article 2 to RIGEL.

5.4 RIGEL agrees that nothing in this Agreement grants RIGEL any express or implied license or right under or to:

(a) U.S. Patent 4,656,134, entitled "Amplification of Eucaryotic Genes" or any patent application corresponding thereto; or

(b) U.S. Patent 5,070,012, entitled "Monitoring of Cells and Trans-Activating Transcription Elements" or any patent application corresponding thereto; or

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(c) U.S. Patent 5,804,387, entitled "FACS-Optimized Mutants of the Green Fluorescent Protein (GFP) or any patent application corresponding thereto.

5.5 STANFORD agrees that nothing in this Agreement grants STANFORD any express or implied license or right under or to U.S. Patent Application Nos. 08/789,333, 08/589,911, or 08/963,368, entitled "Method for Screening for Transdominant Intracellular Effector Peptides and RNA Molecules," or any continuations, divisionals or continuation-in-parts thereof or any patents which may issue therefrom.

5.6 Except as provided in Sections 5.1, 5.2 and 5.3 and as otherwise expressly set forth in this Agreement, nothing in this Agreement will be construed as a warranty or representation that anything made, used, sold, or otherwise disposed of under any license granted in this Agreement is or will be free from infringement of patents, copyrights, and trademarks of third parties; conferring rights to use in advertising, publicity, or otherwise any trademark or the name of "STANFORD"; or granting by implication, estoppel, or otherwise any licenses or rights under patents of STANFORD.

5.7 EXCEPT AS EXPRESSLY SET FORTH IN THE AGREEMENT, STANFORD MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED. THERE ARE NO EXPRESS OR IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR THAT THE USE OF THE LICENSED BIOLOGICAL MATERIALS OR LICENSED KNOW-HOW WILL NOT INFRINGE ANY PATENT, COPYRIGHT, TRADEMARK, OR OTHER RIGHTS, OR ANY OTHER EXPRESS OR IMPLIED WARRANTIES.

6. INDEMNITY.

6.1 RIGEL agrees to indemnify, hold harmless, and defend STANFORD, UCSF-Stanford Health Care and Stanford Health Services and their respective trustees, officers, employees, students, and agents against any and all claims by third parties for death, illness, personal injury, property damage, and improper business practices arising out of the manufacture, use, sale, or other disposition of the Licensed Biological Materials or any products arising or derived from Licensed Biological Materials, by RIGEL or RIGEL's sublicensee(s) or customers.

6.2 STANFORD shall not be liable for any indirect, special, consequential or other damages whatsoever, whether grounded in tort (including negligence), strict liability, contract or otherwise. STANFORD shall not have any responsibilities or liabilities whatsoever with respect to products arising or derived from Licensed Biological Materials by RIGEL.

6.3 RIGEL shall at all times comply, through insurance or self-insurance, with all statutory workers' compensation and employers' liability requirements covering any and all employees with respect to activities performed under this Agreement.

6.4 In addition to the foregoing, RIGEL shall maintain Comprehensive General Liability Insurance, including Products Liability Insurance, with reputable and financially secure

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insurance carrier(s) to cover the activities of RIGEL and its sublicensee(s) in the amounts and during the periods specified herein. Such insurance shall provide minimum limits of liability of One Million Dollars ($1,000,000) as of

the first anniversary of the date upon which RIGEL first leases a facility in which it will conduct research and development activities, and of Five Million Dollars ($5,000,000) as of the commencement of human clinical trials. Such insurance shall include STANFORD, UCSF-Stanford Health Care and Stanford Health Services, their trustees, directors, officers, employees, students, and agents as additional insureds. Such insurance shall be written to cover claims incurred, discovered, manifested or made during or after the expiration of this Agreement. At STANFORD's request, RIGEL shall furnish a Certificate of Insurance evidencing primary coverage and requiring thirty (30) days prior written notice of cancellation or material change to STANFORD. RIGEL shall advise STANFORD, in writing, that it maintains excess liability coverage (following form) over primary insurance for at least the minimum limits set forth above. All such insurance of RIGEL shall be primary coverage; insurance of STANFORD, UCSF-Stanford Health Care or Stanford Health Services shall be excess and noncontributory.

7. STANFORD NAMES AND MARKS.

RIGEL agrees not to identify STANFORD in any promotional advertising or other promotional materials to be disseminated to the pubic or any portion thereof or to use the name of any STANFORD faculty member, employee, or student or any trademark, service mark, trade name, or symbol of STANFORD, UCSF-Stanford Health Care or Stanford Health Services, or that is associated with any of them, without STANFORD's prior written consent, except as required by law. STANFORD shall not unreasonably withhold consent under this Section 7.

8. SUBLICENSE(S).

8.1 Subject to the provisions of this Article 8, RIGEL may grant a sublicense to the license rights granted to RIGEL by STANFORD in Sections 2.1 and 2.2 to Cell Genesys solely in the field of human and/or animal gene therapy.

8.2 Any sublicense granted by RIGEL to Cell Genesys under this Agreement shall be subject and subordinate to terms and conditions of this Agreement, except:

(a) Sublicense terms and conditions shall reflect that any sublicensee(s) shall not grant a sublicense to a third party; and

(b) The financial obligations of any sublicensee to RIGEL specified in the sublicense(s) may be different from those obligations set forth in this Agreement.

Any such sublicense(s) also shall expressly include the provisions of Articles 5 and 6 for the benefit of STANFORD and shall survive any termination of this Agreement.

8.3 RIGEL agrees to provide STANFORD with a copy (with financial terms redacted) of any sublicense granted to Cell Genesys pursuant to this Article 8 and written notice

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of the effective date of any termination of such sublicense prior to the expiration of the Term (as defined in Section 9.1).

9. TERM AND TERMINATION.

9.1 The term of this Agreement shall commence upon the Effective Date and shall expire upon the later of: (a) the expiration of the last to expire of any Patents owned by STANFORD at any time which claim inventions in the Licensed Biological Materials or the Licensed Know-How; or (b) twenty (20) years from the Effective Date (the "Term"). In addition, RIGEL may terminate this Agreement prior to the expiration of the Term by giving STANFORD notice in writing at least thirty (30) days in advance of the effective termination date selected by RIGEL.

9.2 Either party may terminate this Agreement prior to the expiration of the Term if the other party is in material breach of any provision hereof and fails to remedy any such default or breach within thirty (30) days after written notice thereof to the breaching party.

9.3 Surviving the expiration of the Term are:

(a) Any cause of action or claim of RIGEL or STANFORD, accrued or to accrue, because of any breach or default by the other party prior to the expiration of the Term; and

(b) Articles 4, 5, 6, 7 and 11; and

(c) Article 8 and Sections 2.1 and 2.2; and the licenses granted thereunder shall be deemed perpetual and fully paid-up.

9.4 Surviving any termination of this Agreement are:

(a) Any cause of action or claim of RIGEL or STANFORD, accrued or to accrue, because of any breach or default by the other party prior to the termination of this Agreement; and

(b) Articles 4, 5, 6, 7, 8 and 11 and Section 3.2; and

(c) Sections 2.1 and 2.2 if RIGEL has fulfilled all of its payment obligations to STANFORD under Section 3.1 prior to such termination; and the licenses granted thereunder shall be deemed perpetual and fully paid-up.

10. ASSIGNMENT.

This Agreement may not be assigned by either party without the express written consent of the other party, except that RIGEL may assign the Agreement in connection with a merger, consolidation or sale of all or substantially all of RIGEL's assets.

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11. ARBITRATION.

11.1 Any controversy arising under or related to this Agreement, and any disputed claim by either party against the other under this Agreement excluding any dispute relating to patent validity or infringement arising under this Agreement, shall be settled by arbitration in accordance with the Licensing Agreement Arbitration Rules of the American Arbitration Association.

11.2 Upon request by either party, arbitration will be by a third party arbitrator mutually agreed upon in writing by RIGEL and STANFORD within thirty (30) days of such arbitration request. Judgment upon the award rendered by the arbitrator shall be final and nonappealable and may be entered in any court having jurisdiction thereof.

11.3 The parties shall be entitled to discovery in like manner as if the arbitration were a civil suit in the California Superior Court.

11.4 Any arbitration shall be held at Stanford, California, unless the parties hereto mutually agree in writing to another place.

12. NOTICES.

All notices under this Agreement shall be deemed to have been fully given when done in writing and deposited in the United States mail registered or certified, and addressed as follows:

To STANFORD:
Office of Technology Licensing
Stanford University
900 Welch Road, Suite 350
Palo Alto, CA 94304-1850
Attention: Director

To RIGEL:
Rigel Pharmaceuticals, Inc.
240 East Grand Ave.
South San Francisco, CA 94080
Attention: President

Either party may change its address upon written notice to the other party.

13. WAIVER.

None of the terms of this Agreement can be waived except by the written consent of the party waiving compliance.

14. APPLICABLE LAW.

This Agreement shall be governed by the laws of the State of California applicable to agreements negotiated, executed and performed wholly within California. Any claim or controversy arising out of or related to this Agreement or any breach hereof shall be submitted to a court of applicable

jurisdiction in the State of California, and each party hereby consents to the

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jurisdiction and venue of such court.

15. DISCLAIMER OF AGENCY.

Neither party is, or will be deemed to be, the legal representative or agent of the other, nor shall either party have the right or authority to assume, create, or incur any third party liability or obligation of any kind, express or implied, against or in the name of or on behalf of another except as expressly set forth in this Agreement.

16. SEVERABILITY.

If any provision or provisions of this Agreement shall be held to be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not be in any way affected or impaired thereby.

17. ENTIRE AGREEMENT.

This Agreement, together with the Exhibit attached hereto, embodies the entire understanding of the parties and shall supersede all previous communications, representations or understandings, either oral or written, between the parties relating to the subject matter hereof. No amendment or modification hereof shall be valid or binding upon the parties unless made in writing and signed by duly authorized representatives of both parties.

18. COUNTERPARTS.

This Agreement may be executed in counterparts, with the same force and effect as if the parties had executed the same instrument.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement in duplicate originals by their duly authorized officers or representatives.

THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY	RIGEL PHARMACEUTICALS, INC.
By: /s/ Katherine Ku	By: /s/ Donald W. Perryman
Name: Katherine Ku	Name: Donald W. Perryman
Title: Director, Technology Licensing	Title: VP, Business Development June 9, 1999

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EXHIBIT A

LICENSED BIOLOGICAL MATERIALS

[*] Vectors:

[*]

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APPENDIX F

Application, Patent Number or Publication Number	Filing Date, Grant Date, or Publication Date	Title/Inventors
[*]	[*]	[*]
[*]	[*]	[*]
[*]	[*]	[*]
[*]	[*]	[*]
[*]	[*]	[*]
[*]	[*]	[*]
[*]	[*]	[*]
[*]	[*]	[*]

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APPENDIX G
RESEARCH PLAN
[*]
(6 pages of text omitted here)

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APPENDIX H
LIST OF FTEs
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APPENDIX I
THIRD PARTY PATENTS
[*]

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Exhibit 10.10

COLLABORATIVE RESEARCH AND DEVELOPMENT AGREEMENT

This Agreement is entered into as of December , 1997 (the "Effective Date"), by and between NEUROCRINE BIOSCIENCES INC., a Delaware corporation having an office at 3050 Science Park Road, San Diego, California 92121 ("Neurocrine"), and RIGEL, INC., a Delaware corporation having an office at 772 Lucerne Drive, Sunnyvale, California 94086 ("Rigel").

RECITALS

WHEREAS, Neurocrine has an active research program in the area of neurodegeneration and has developed a substantial compound library and drug screening and medicinal chemistry capabilities;

WHEREAS, Rigel has certain intellectual property and expertise pertaining to the discovery, and identification of molecular targets associated with signal transduction pathways; and

WHEREAS, Neurocrine and Rigel desire to establish a collaboration for the discovery, development and commercialization of (a) novel protein targets involved in glial cell and macrophage activation, and (b) small molecule inhibitors of protein:protein interactions involving proteins other than those involved in glial cell activation (the "Collaboration"), and to reflect their mutual understanding within this definitive Collaborative Research and Development Agreement (the "Collaboration Agreement" or the "Agreement");

NOW, THEREFORE, in consideration of the foregoing and the covenants and promises contained in this Collaborative Agreement, the parties agree as follows:

AGREEMENT

I. DEFINITIONS

1.1 "AFFILIATE" means, as to a party to this Agreement, any corporation, company, partnership, joint venture or other entity which controls, is controlled by, or is under common control with, such party. For purposes of this Section 1.1, control shall mean (without limitation) in the case of corporate entities, the direct or indirect ownership of at least fifty percent (50%) of the stock or participating shares entitled to vote for the election of directors.

1.2 "ANNUAL RESEARCH PLAN" means a plan approved by the Steering Committee detailing the scope, level and extent of the Research and Development, the specific technical and scientific responsibilities of each party for each party for each one-year period during the Research and Development Period, as described in Section 3.2.

1.3 "COLLABORATION PRODUCTS" means collectively, Rigel Collaboration Products and Neurocrine Collaboration Products.

1.4 "CONFIDENTIAL INFORMATION" means any proprietary information, including the Neurocrine Technology and Rigel Technology, and any other information relating to any research project, work in process, future development, scientific, manufacturing, marketing, business plan, financial or personnel matter relating to either party, its present or future products, sales, suppliers, customers, employees, investors or business that one party discloses to the other party during the term of this Agreement, whether in oral, written, graphic or electronic form.

1.5 "DEVELOPMENT MOLECULES" means any small molecule included in the Neurocrine library or produced in the course of Neurocrine's performance of medicinal chemistry on a small molecule included in the Neurocrine Chemical Library pursuant to Section 2.3, which small molecule is screened against a Rigel Target and is determined by the Research Committee to have an EC(50) of less than 1 uM against such target. Development Molecules exclude Peptide Antagonists.

1.6 "EUROPE" shall mean the United Kingdom, Germany, France, Italy, Spain and Switzerland.

1.7 "JOINT TECHNOLOGY" means any and all discoveries, modifications, improvements, know-how, trade secrets, inventions (whether or not patentable), patent applications and patents (including, without limitation,

all substitutions, divisionals, reissues, reexaminations, continuations, continuations-in-part and inventors' certificates and all foreign counterparts of the foregoing), data, information or physical, chemical or biological material useful or necessary to the development or commercialization of Collaboration Products that is developed by Neurocrine and Rigel jointly during the term of this Agreement as a result of Research and Development under the Annual Research Plan. Ownership of Joint Technology shall be determined in accordance with Article 6.

1.8 "MAJOR COUNTRIES" means the United States, Europe, Japan and Canada.

1.9 "NEUROCRINE CHEMICAL LIBRARY" means the library of chemical compounds that Neurocrine owns or controls during the Research and Development Period. For the purposes of this Agreement, the Neurocrine Chemical Library shall be assumed to be approximately one hundred thousand (100,000) compounds during the first year of the Collaboration, and approximately one hundred twenty-five thousand (125,000) compounds during the second year of the Collaboration, and shall be deemed to exclude any compounds that Neurocrine has licensed to a third party prior to the Effective Date and any compounds that Neurocrine is precluded from providing to Rigel under this Agreement by reason of contractual or other proprietary flights of a third party.

1.10 "NEUROCRINE COLLABORATION PRODUCTS" means any product incorporating or discovered utilizing a Protein Target or a Peptide Antagonist.

1.11 "NEUROCRINE TECHNOLOGY" means any and all discoveries, modifications, improvements, know-how, trade secrets, inventions (whether or not patentable), patent

applications and patents (including, without limitation, all substitutions, divisionals, reissues, reexaminations, continuations, continuations-in-part and inventors' certificates and all foreign counterparts of the foregoing), data, information or physical, chemical or biological material useful or necessary to the development or commercialization of Collaboration Products that is owned or licensed (with a right to sublicense) by Neurocrine as of the Effective Date or solely made or developed by Neurocrine during the Research and Development of Collaboration Products pursuant to this Agreement.

1.12 "PROTEIN TARGET" means an enzyme, receptor, transducer or transcription factor or other molecule identified during the performance of the Research and Development that the Research Committee determines, based upon data generated during the Research and Development, is a molecule primarily involved in glial cell activation. Protein Targets shall exclude Rigel Targets.

1.13 "PARTY" means Neurocrine or Rigel or their respective Affiliates.

1.14 "PEPTIDE ANTAGONISTS" means peptides identified or produced by Rigel pursuant to Section 2 that the Research Committee determines, based upon data generated during the Research and Development, to have activity against one or more Protein Targets. Peptide Antagonists exclude Development Molecules.

1.15 "RESEARCH AND DEVELOPMENT" means the collaborative activities conducted by the parties during the Research and Development Period pursuant to this Agreement targeted toward the generation, identification, production and characterization of Rigel Targets, Protein Targets, Peptide Antagonists and Development Molecules.

1.16 "RESEARCH AND DEVELOPMENT PERIOD" means the period commencing upon the Effective Date and terminating upon the second anniversary of the Effective Date, during which period the parties shall conduct Research and Development. The parties may extend the Research and Development Period for additional one (1) year periods upon mutually acceptable terms.

1.17 "RIGEL COLLABORATION PRODUCTS" means any product incorporating or discovered utilizing Rigel Target or a Development Molecule.

1.18 "RIGEL TARGET" means an enzyme, receptor, transducer, transcription factor or other molecule that the Research Committee determines, based upon data generated during the Research and Development, is specifically associated primarily with processes other than glial cell activation. Rigel Targets exclude Protein Targets.

1.19 "RIGEL TECHNOLOGY" means any and all discoveries, modifications, improvements, know-how, trade secrets, inventions (whether or not patentable), patent applications and patents (including, without limitation, all substitutions, divisionals, reissues, reexaminations, continuations,

continuations-in-part and inventors' certificates and all foreign

counterparts of the foregoing), data, information or physical, chemical or biological material useful or necessary to the development or commercialization of Collaboration Products that is owned or licensed (with a right to sublicense) by Rigel as of the Effective Date or solely made or developed by Rigel during the Research and Development of Collaboration Products performed pursuant to this Agreement.

1.20 "STEERING COMMITTEE" means the committee established under Section 3 of this Agreement.

2. RESEARCH AND DEVELOPMENT COLLABORATION

2.1 OVERVIEW. The primary purpose of the Collaboration is to conduct Research and Development toward the discovery and development of Collaboration Products in accordance with the Annual Research Plan. To that end, it is contemplated by the parties that:

(a) Neurocrine will have primary responsibility for supplying certain cell lines necessary for the study of glial cell activation, providing small molecule compounds from the Neurocrine Chemical Library, performing limited medicinal chemistry as required by the Annual Research Plan, and conducting certain screening and secondary assays and screening compounds from the Neurocrine Chemical Library against Rigel Targets;

(b) Neurocrine and Rigel will share responsibility for applying the Rigel Technology to develop an appropriate glial cell assay system to identify Protein Targets and Peptide Antagonists; and

(c) Rigel will have primary responsibility for identifying and providing Protein Targets, identifying and sequencing gene(s) coding for the Protein Targets, and generating, identifying and providing Peptide Antagonists of such Protein Targets. Rigel will also have responsibility for providing Rigel Targets to Neurocrine for screening purposes. It is understood that the individual and joint responsibilities will be set forth in detail in the Annual Research Plan to be developed pursuant to Section 3.2.

2.2 IDENTIFICATION AND TRANSFER OF PROTEIN TARGETS. The parties shall use diligent efforts to identify and transfer to Neurocrine one or more "primary" Protein Targets that the Research Committee determines, based upon the activity of such target in glial cell function assays performed during the Research and Development, to be the best targets against which to screen small molecules for activity. To this end, within the first year of the Collaboration, Rigel shall use diligent efforts to identify and provide to Neurocrine at least six (6) Protein Targets, the genes encoding those Protein Targets, and Peptide Antagonists active against such Protein Targets, unless the Steering Committee otherwise provides in the Annual Research Plan. In the event that Rigel is unable, using such diligent efforts, to provide the Protein Targets, genes encoding the Protein Targets and/or Peptide Antagonists within the first year of the Collaboration, Rigel shall continue to use diligent efforts to provide such biological materials as soon as possible thereafter.

2.3 TRANSFER OF DEVELOPMENT MOLECULE TECHNOLOGY.

(a) Within the first year of the Collaboration, Rigel may provide to Neurocrine a maximum of three (3) Rigel Targets that Neurocrine shall screen against the Neurocrine Chemical Library. Similarly, during the second year of the Collaboration, Rigel may provide to Neurocrine a maximum of another three (3) Rigel Targets for the purposes of screening against the Neurocrine Chemical Library. In no instance shall Neurocrine be obligated to screen a Rigel Target that it believes in good faith to be in direct competition with a Neurocrine research and development program existing at the time of the request. All Rigel Targets shall be formatted in 96-well plates in an assay suitable for high throughput screening. Within six (6) months of receipt of a Rigel Target, Neurocrine shall screen such Rigel Targets as directed by the Research Committee and provide Rigel with the results of such screen. In the event Rigel provides more than two Rigel Targets to Neurocrine in any sixty (60) day period, Neurocrine shall have the right to extend the time period within which it must provide the results of the screen by an additional sixty (60) days.

(b) Based upon the results of the foregoing screening activities, Rigel may select one (1) Rigel Target in each of the two years of the

Research and Development Period. During the second year of the Collaboration, Neurocrine shall devote one full-time equivalent (FTE) for the purpose of performing medicinal chemistry on molecules in the Neurocrine Chemical Library that the Research Committee determines are active against the Rigel Target and most suitable for structure-activity relationship development, and perform additional appropriate screening to provide Rigel with a Development Molecule prior to expiration of the Research and Development Period. Once a Development Molecule has been identified, Neurocrine shall no longer be obligated to expend any additional effort or resources on such Rigel Target or Development Molecule. In the event that Neurocrine, in its discretion, determines that it is unable to devote the services of one full-time equivalent (FTE) to such medicinal chemistry activities during the second year of the Collaboration, Neurocrine may elect to provide Rigel with a portion of the Neurocrine Chemical Library (hereinafter the "Sample Library") in lieu of the performance of such services. The Sample Library shall consist of approximately one hundred microliters (100 uL) of a ten millimolar (10mM) stock solution of any compound then existing in the Neurocrine Chemical Library, for which Neurocrine has in its possession a quantity of at least 2 milligrams, on a compound-by-compound basis. The Sample Library shall also include any structural information Neurocrine has in its possession with regard to the transferred compounds. At the end of the second year of the Collaboration (or earlier as provided above), Neurocrine shall provide to Rigel the Sample Library to allow Rigel to conduct internal screening activities, excluding the screening of any targets which Neurocrine is, or reasonably anticipates, itself screening, as determined at the time of transfer. For purposes of clarity, at the time of transfer Neurocrine shall provide Rigel with a list of the targets as to which screening of the Sample Library is prohibited.

2.4 CONDUCT OF RESEARCH AND DEVELOPMENT. The parties will conduct their respective Research and Development activities under the Annual Research Plan in good

scientific manner and in compliance with all applicable governmental, regulatory and legal requirements. Neurocrine and Rigel will each use their good faith scientific and business judgment to allocate sufficient time, effort, equipment and facilities to. the Collaboration to achieve the objectives of the Collaboration consistent with the terms of this Agreement and the recommendations of the Steering Committee, as provided in Section 3 below.

2.5 VISIT OF FACILITIES. Representatives of either party may, upon reasonable notice and at a frequency reasonably acceptable to the Other party during normal business hours (a) visit the facilities where the Research and Development is being conducted; and (b) consult informally, during such visits and by telephone, with personnel of the other party performing the Research and Development. Each party shall bear its own expenses with regard to any such visits. If requested by the other party, Neurocrine and Rigel shall cause appropriate individuals working on the Research and Development to be available for meetings at the location of the facilities where such individuals are employed at times reasonably convenient to each party.

2.6 DISCLOSURE OF DATA. The parties will promptly provide to each other all data generated during the Research and Development, including, without limitation, all Neurocrine Technology, Joint Technology and Rigel Technology arising during the Research and Development Period.

3. STEERING COMMITTEE

3.1 FORMATION. The parties will promptly after the Effective Date form a Steering Committee having six members, with an equal number of representatives from each of Neurocrine and Rigel. Each party may replace its respective representatives on the Steering Committee from time to time upon written notice to the other party.

3.2 MEETING AND RESPONSIBILITIES.

(a) Within ninety (90) days from execution of this Agreement, the Steering Committee shall formulate and approve an Annual Research Plan which shall guide each party's activities through December 31, 1998. The Steering Committee will meet regularly during the Research and Development Period to: (i) set objectives for the Research and Development; (ii) assess the level and extent of the Research and Development activities to be conducted by each party; (iii) review the progress of the Research and Development; (iv) oversee patent matters relating to Joint Technology and any Rigel Technology or Neurocrine Technology to be assigned pursuant to Section 6.3; (v) ensure that the designation of all Rigel Targets, Protein Targets, Peptide Antagonists and

Development Molecules is documented and is consistent with the definitions provided herein, and resolve any disputes regarding such designations; (vi) oversee the extent and timing of any technology transfer necessary or appropriate for the Research and

Development; and (vii) encourage and facilitate ongoing cooperation between the parties. Meetings of the Steering Committee will take place at mutually agreed upon times and locations. From time to time, the Steering Committee may establish subcommittees (including a Research Committee responsible for directing the parties' day to day Research and Development activities) to oversee particular projects or activities, and such additional subcommittees shall be staffed as designated by the Steering Committee.

(b) By September 1, 1998, Neurocrine and Rigel shall submit to one another their respective proposals concerning the Research and Development to be conducted during the next calendar year. Thereafter, Neurocrine and. Rigel shall jointly prepare proposed revisions to the draft Annual Research Plan for submission to the Steering Committee for approval. The Steering Committee shall review the proposal as soon as possible after receipt, and shall establish and approve a final Annual Research Plan for the following calendar year prior to or on November 15, 1998. The Steering Committee may amend the Annual Research Plan from time to time as it deems necessary or appropriate. The parties shall alternate the responsibility of preparing and distributing the minutes of such Steering Committee meetings, with Neurocrine preparing the minutes of the first meeting. All such meeting minutes should, whenever possible, be distributed to the parties within twenty-one (21) days from the date of the meeting, and should include any changes to the Annual Research Plan, and a summary of any inventions, discoveries or results achieved under this Agreement which should be deemed to be Joint Technology. If necessary or desired, each party may consult with its respective patent counsel prior to rendering any such designation of results as Joint Technology. The Steering Committee shall attempt to resolve any disagreements regarding whether a given technology should be designated as Joint Technology, Rigel Technology or Neurocrine Technology pursuant to Section 6.6.

3.3 DISAGREEMENTS. Decisions of the Steering Committee shall be by a majority vote. If no majority vote is obtained with respect to any issue, the matter will be referred to the Chief Executive Officer of each party or such other senior executive designated by a party who is reasonably acceptable to the other party and who has decision-making authority. Such persons shall meet and attempt to resolve the matter in good faith. Any disputes that remain unresolved by such executives shall be submitted for resolution as provided in Section 9.3.

4. COLLABORATION FUNDING

4.1 RESEARCH AND DEVELOPMENT FUNDING. Neurocrine and Rigel shall each be responsible for their own costs associated with activities within the Annual Research Plan.

5. LICENSES

5.1 RESEARCH LICENSE TO RIGEL. Neurocrine hereby grams to Rigel a non-exclusive, worldwide, royalty-free license, without the right to sublicense, under Neurocrine's interest in the Neurocrine Technology, Joint Technology and any Rigel Technology that may be assigned to Neurocrine pursuant to Section 6.5, solely to the extent necessary or appropriate for Rigel to conduct Research and Development of Collaboration Products pursuant to this Agreement.

5.2 RESEARCH LICENSE TO NEUROCRINE. Rigel hereby grants to Neurocrine a non-exclusive, worldwide, royalty-free license, without the right to sublicense, under Rigel's interest in the Rigel Technology, Joint Technology and any Neurocrine Technology that may be assigned to Rigel pursuant to Section 6.5, solely to the extent necessary or appropriate for Neurocrine to conduct Research and Development of Collaboration Products pursuant to this Agreement.

5.3 COMMERCIALIZATION LICENSE TO NEUROCRINE. Rigel hereby grants to Neurocrine an exclusive, worldwide, royalty free license, with the right to sublicense, under Rigel's interest in any applicable intellectual property

rights within the Rigel Technology or the Joint Technology solely to develop, make, use, sell, offer for sale and import Neurocrine Collaboration Products.

5.4 COMMERCIALIZATION LICENSE TO RIGEL. Neurocrine hereby grants to Rigel an exclusive, worldwide, royalty-free, license, with the right to sublicense, under Neurocrine's interest in any applicable intellectual property rights within the Neurocrine Technology or the Joint Technology solely to develop, make, use, sell, offer for sale or import Rigel Collaboration Products.

6. PATENT MATTERS

6.1 OWNERSHIP. Subject to Section 6.5, as determined in accordance with the rules of inventorship under U.S. law, each party shall have sole ownership of all inventions made solely by its employees or other agents during the term of this Agreement, which inventions shall be Rigel Technology if made solely by Rigel's employees or agents or Neurocrine Technology if made solely by Neurocrine's employees or agents. The parties shall each own a fifty percent (50%) undivided interest (without accounting) in all inventions made jointly by the parties' employees or other agents, subject to any licenses granted pursuant to this Agreement, which inventions shall be Joint Technology. Specifically, Neurocrine shall have sole ownership and control of the Neurocrine Technology, and Rigel shall have sole ownership and control of Rigel Technology, subject to any licenses granted pursuant to this Agreement. The parties agree that they each shall enter into agreements with their respective employees and other agents providing

that, to the maximum extent permitted by applicable law, such employees and other agents shall assign (or be obligated to assign) to the party hereto which acts as their employer or principal, the ownership and control of all inventions conceived or reduced to practice by such employees and agents in the course of their employment for, or within the scope of the agency relationship with, each party hereto. Any disputes regarding the designation of inventions as Neurocrine Technology, Rigel Technology or Joint Technology shall be submitted for resolution by the Steering Committee.

6.2 PROSECUTION OF PATENTS CONSTITUTING RIGEL TECHNOLOGY. Rigel shall prepare, file, prosecute and maintain patent applications and/or patents worldwide, in accordance with Section 6.6, for those inventions within the Rigel Technology and any inventions assigned to Rigel pursuant to Section 6.5. Rigel shall use its best efforts, consistent with its own internal filing procedures, to obtain letters patent on patentable Rigel Technology in all Major Countries and, where possible and appropriate, worldwide.

6.3 PROSECUTION OF PATENTS CONSTITUTING NEUROCRINE TECHNOLOGY AND JOINT TECHNOLOGY. Neurocrine shall prepare, file, prosecute and maintain patents and/or patent application worldwide, in accordance with Section 6.6, for those inventions within the Neurocrine Technology and within the Joint Technology and any inventions included in the Rigel Technology that are assigned to Neurocrine pursuant to Section 6.5. Neurocrine shall use its best efforts, consistent with its own internal filing procedures, to obtain letters patent in all Major Countries and, where possible and appropriate, worldwide.

6.4 COOPERATION IN PATENT MATTERS. Consistent with Section 6.6 below, the parties agree to cooperate with each other as necessary or appropriate in the preparation, filing and prosecution of patent applications pursuant to Sections 6.2, 6.3 and 6.5, including providing one another a reasonable opportunity to review and comment on any patent application to be filed in the U.S. or in any other country. All costs associated with the preparation, filing, prosecution and maintenance of patent applications and patents coveting jointly owned Joint Technology shall be shared equally by the parties.

6.5 TRANSFER OF CERTAIN PATENTS CONSTITUTING NEUROCRINE TECHNOLOGY, RIGEL TECHNOLOGY OR JOINT TECHNOLOGY. Notwithstanding Sections 6.1 and 6.2, Rigel shall assign its interest in any inventions included in the Rigel Technology and any Joint Technology that is solely related to a Protein Target or to a Peptide Antagonist to Neurocrine, and Neurocrine shall thereafter prepare, file, prosecute and maintain patents and/or patent applications worldwide for all such inventions, consistent with the provisions of Section 6.3. Similarly, notwithstanding Sections 6.1 and 6.3, Neurocrine shall assign its interest in any invention included in the Neurocrine Technology and any Joint Technology that is solely related to a Development Molecule or to a Rigel Target to Rigel, and Rigel shall thereafter prepare, file, prosecute and maintain patents and/or patent applications worldwide for all such inventions, consistent with the

provisions of Section 6.2.

6.6 DISCLOSURE OF INVENTIONS AND REVIEW OF PATENT APPLICATIONS. Each party shall provide the other with a copy of a summary of any disclosure of an invention (including those inventions included in the Joint Technology) arising in the course of the Collaboration as soon as is reasonably practical after such party recognizes such invention to allow the other party an opportunity to comment upon the subject matter and upon the ownership and inventorship of the invention. Subsequent to the provision of such a summary, designation of an invention as Rigel Technology, Neurocrine Technology or Joint Technology, and the determination of the ownership of such invention, the party responsible for filing a patent application on such invention pursuant to Section 6 shall provide the other party with a copy of any draft patent application directed toward the invention in order. In addition, Neurocrine shall provide to Rigel a copy of all amendments or substantive communications relating to jointly owned Joint Technology sufficiently in advance of any relevant deadline or anticipated submission date to allow Rigel a reasonable opportunity to evaluate and comment upon any such application, amendment or substantive communication.

6.7 ENFORCEMENT OF PATENTS BY A SINGLE PARTY. (a) Rigel shall have the first right (but not the obligation) to enforce the patents included in the Rigel Technology and any patents included in the Neurocrine Technology or Joint Technology that are assigned to Rigel pursuant to section 6.4 against third party infringement, and (b) Neurocrine shall have the first right (but not the obligation) to enforce the patents included within the Neurocrine Technology or Joint Technology (other than those patents included in the Joint Technology or Neurocrine Technology that are assigned to Rigel pursuant to Section 6.5) against third party infringement. In the event that the party with the first right to enforce a patent pursuant to this Section 6.6 fails to commence enforcement or otherwise terminates the alleged infringement within six months after that party has learned of the alleged infringement, the other party shall have the right, but not the obligation, to bring and control any such action using counsel of its own choice and at its own expense.

6.8 JOINT ENFORCEMENT OF PATENTS. If one party commences enforcement proceedings pursuant to Section 6.6, the other party may elect upon written notice to the enforcing party to join in the action in order to provide reasonable assistance and to share in the costs and expenses associated with the action. Any monetary awards recovered through the action shall first be applied to fees and expenses, and the remainder shared pro rata based upon the relative financial contribution of the parties to such fees and expenses.

6.9 THIRD PARTY INFRINGEMENT ACTIONS. If a party receives notice of any suit or claim alleging that the conduct of the activities within this Agreement infringes the proprietary rights of a third party, the parties shall promptly meet to discuss and decide on an appropriate response.

7. CONFIDENTIALITY

7.1 CONFIDENTIALITY OBLIGATION. During the term of this Agreement and for a period of five years thereafter, each party hereto shall maintain in confidence all Confidential Information disclosed to it by the other party. Neither party will use, disclose or grant the use of such Confidential Information except as expressly authorized by this Agreement. To the extent that disclosure is authorized by this Agreement, the disclosing party will obtain prior agreement from its employees, agents, consultants or investigators to whom disclosure is to be made to hold in confidence and not make use of such information for any purpose other than those permitted by this Agreement. Each party will use at least the same standard of care as it uses to protect its own proprietary and trade secret information to ensure that such employees, agents, consultants and investigators do not disclose or make any unauthorized use of such Confidential Information. Each party will promptly notify the other upon discovery of any unauthorized use or disclosure of the Confidential Information.

7.2 EXCEPTIONS. The obligations of confidentiality contained in Section 7.1 will not apply to the extent that it can be established by the party receiving Confidential Information (the "Receiving Party") by competent proof that such Confidential Information:

(a) was already known to the Receiving Party, other than under an obligation of confidentiality with respect thereto, at the time of receipt from the other party;

(b) was generally available to the public or otherwise part of the public domain at the time of its receipt from the other party;

(c) becomes generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the Receiving Party in breach of this Agreement; or

(d) was received by the Receiving Party, other than under an obligation of confidentiality, by a third party without breach of any obligations of confidentiality with respect thereto.

7.3 AUTHORIZED DISCLOSURE. Each party may disclose the Confidential Information to the extent such disclosure is reasonably necessary in filing or prosecuting patent applications, prosecuting or defending litigation, or complying with applicable laws, governmental regulations, or court orders provided that if such party is required to make any such disclosure of the Confidential information it will to the extent practicable give reasonable advance notice to the other party of such disclosure requirement and, except to the extent inappropriate in the case of patent applications, will use all reasonable efforts to secure confidential treatment of such information required to be disclosed, subject to the limitations on disclosure set forth in Section 7.4 (b).

7.4 PUBLICATION.

(a) During the term of this Agreement and for a period of five (5) years thereafter, Neurocrine and Rigel each acknowledge the other party's interest in publishing certain of its results to obtain recognition within the scientific community and to advance the state of scientific knowledge. Each party also recognizes the mutual interest in obtaining valid patent protection and maintaining as confidential any Confidential Information or non-patentable information which would have commercial value when undisclosed and maintained as a trade secret. Consequently, if a party, its employees or consultants desire to make a disclosure (including both written publications and oral presentations made in the absence of a contractual obligation of confidentiality) relating to work performed by such party (the "Publishing Party") as part of the Research and Development, it shall transmit to the other party (the "Reviewing Party") a copy of the proposed written publication at least sixty (60) days prior to submission for publication, or an outline of such oral presentation at least thirty (30) days prior to the anticipated date of presentation. The Reviewing Party shall have the right (i) to propose modifications to the publication or presentation to protect the patentability of inventions, to maintain a trade secret or to protect other Confidential Information of a party and (ii) to request a delay in publication or presentation for a reasonable period of time as provided in Section 7.4(b) in order to protect patentable information.

(b) If the Reviewing Party requests such a delay, the Publishing Party shall delay the submission of the publication or the oral presentation for a period of up to ninety (90) days to allow one or both parties to file patent applications coveting information included in the publication or presentation in accordance with Section 6. If the Reviewing Party reasonably claims that such information, whether patentable or not, either is Confidential Information of the Reviewing Party or may have significant commercial value and can be maintained as a trade secret, the Publishing Party shall publish or disclose only such information which would not adversely affect the confidentiality of such Confidential Information or the commercial value of such trade secret. Upon the expiration of sixty (60) or thirty (30) day review period (as the case may be) set forth in Section 7.4(a), the Publishing Party shall be free to proceed with the written publication or the presentation, as applicable, unless the Reviewing Party has requested a further delay or a modification described in this Section 7.4(b).

8. TERM AND TERMINATION OF THE AGREEMENT

8.1 TERM. Unless earlier terminated as provided below, the term of this Agreement shall commence upon the Effective Date and terminate concurrently With the termination of the Research and Development Period.

8.2 TERMINATION.

(a) Each party will have the right to terminate this Agreement (i) in the event of insolvency or bankruptcy of the other party, or (ii) after written notice to the other that the

other is in breach of any material term of this Agreement, unless the other party cures such breach before the expiration of sixty (60) days from the date of receipt of such notice.

(b) Either party may elect to terminate this Agreement during the Research and Development Period prior to its expiration pursuant to Section 8.1 by providing to the other ninety (90) days written notice. In the event that the Agreement is terminated prior to the second anniversary of the Research and Development Period, the parties will meet and determine in good faith the identity and disposition of all intellectual property rights and biological and chemical materials generated up until the time of termination in accordance with Section 6; provided, however, that the parties will negotiate in good faith the disposition of any intellectual property rights and biological and chemical materials that are not covered by the provisions of Section 6. Expiration or termination of this Agreement shall not relieve the parties of any obligation accruing prior to such expiration or termination.

8.3 EFFECTS OF EXPIRATION OR TERMINATION OF THE RESEARCH AND DEVELOPMENT PERIOD. Upon expiration of the Research and Development Period or any termination of this Agreement prior to the expiration of the Research and Development Period, all remaining chemical and biological materials included in the Rigel Technology that are in Neurocrine's possession at the time of expiration or termination of the Research and Development Period shall be returned to Rigel, and all remaining chemical and biological materials included in the Neurocrine Technology that are in Rigel's possession at the time of expiration or termination of the Research and Development Period shall be returned to Neurocrine, except to the extent that the parties may otherwise agree during discussions conducted pursuant to Section 8.2 (b).

8.4 EFFECTS OF EXPIRATION OR TERMINATION OF THE AGREEMENT. Sections 6, 7, 8, 9.1, 9.2, 9.3, 9.9 and 9.10 shall survive any expiration or termination of this Agreement. Upon any termination of this Agreement prior to its expiration pursuant to Section 8.1. the commercialization licenses granted pursuant to Sections 5.3 and 5.4 shall survive such termination of this Agreement; provided, however, that if this Agreement is terminated for material breach by Neurocrine, then the license granted pursuant to Section 5.3 shall not survive such termination, and further provided that if this Agreement is terminated for material breach by Rigel, then the license granted pursuant to Section 5.4 shall not survive such termination.

9. MISCELLANEOUS PROVISIONS

9.1 INDEMNIFICATION.

(a) Rigel agrees to indemnify, hold harmless and defend the other, its officers, agents, and Affiliates (the "Neurocrine Indemnitees") against any and all claims, suits, losses, damage, costs, fees and expenses of or by third parties (collectively, "Claims") for damage to persons or property resulting directly or indirectly from Rigel's, its Affiliates or its sublicensee's actions in connection with its performance under this Agreement or the manufacture, use, sale offer for sale or import of Rigel Collaboration Products, except to the extent such Claims arise out of or result from the negligence, recklessness or willful acts or omissions of the Neurocrine

Indemnitees or arise out of or result from any breach of this Agreement by the Neurocrine Indemnitee. Any Neurocrine Indemnitee shall give prompt notice to Rigel of any Claims brought or filed against such Neurocrine Indemnitee, and Rigel shall assume the defense of such Claims with counsel reasonably satisfactory to the Neurocrine Indemnitee. Rigel will not be subject to any liability for any settlement of such Claims made by a Neurocrine Indemnitee without Rigel's consent (not to be unreasonably withheld). The Neurocrine Indemnitee may retain separate counsel with respect to any such Claims at its own expense.

(b) Neurocrine agrees to indemnify, hold harmless and defend the other, its officers, agents, and Affiliates (the "Rigel Indemnitees") against any and all claims, suits, losses, damage, costs, fees and expenses of or by third parties (collectively, "Claims") for damage to persons or property resulting directly or indirectly from Neurocrine's, its Affiliates or its sublicensee's actions in connection with its performance under this Agreement or the manufacture, use, sale offer for sale or import of Neurocrine Collaboration Products, except to the extent such Claims arise out of or result from the negligence, recklessness or willful acts or omissions of the Rigel Indemnitees or arise out of or result from any breach of this Agreement by the Rigel Indemnitee. Any Rigel Indemnitee shall give prompt notice to

Neurocrine of any Claims brought or filed against such Rigel Indemnitee, and Neurocrine shall assume the defense of such Claims with counsel reasonably satisfactory to the Rigel Indemnitee. Neurocrine will not be subject to any liability for any settlement of such Claims made by a Rigel Indemnitee without Neurocrine's consent (not to be unreasonably withheld). The Rigel Indemnitee may retain separate counsel with respect to any such Claims at its own expense.

9.2 DISCLAIMER OF WARRANTIES. THE RIGEL TECHNOLOGY AND THE NEUROCRINE TECHNOLOGY ARE PROVIDED BY RIGEL AND NEUROCRINE, RESPECTIVELY, "AS IS" AND EACH PARTY EXPRESSLY DISCLAIMS ALL WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION WARRANTIES OF DESIGN, MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE, NONIFRINGEMENT OF THE INTELLECTUAL PROPERTY RIGHTS OF THIRD PARTIES OR ARISING FROM A COURSE OF DEALING, USAGE OR TRADE PRACTICES WITH RESPECT THERETO. Without limitation, each party expressly does not warrant the success of any Research and Development activities or the safety or usefulness of any technology it provides hereunder.

9.3 DISPUTE RESOLUTION. If a dispute arises between the parties relating to the interpretation or performance of this Agreement or the grounds for the termination thereof, the parties agree to hold a meeting, attended by individuals with decision-making authority regarding the dispute, to attempt in good faith to negotiate a resolution of the dispute prior to pursuing other available remedies. If, within 30 days after such meeting, the parties have not succeeded in negotiating a resolution of the dispute, such dispute shall be submitted to final and binding arbitration under the then current Licensing Agreement Arbitration Rules of the American Arbitration Association ("AAA"), with a panel of three arbitrators with significant experience in the biopharmaceutical industry conducting proceedings in San Diego, California. Such arbitrators

shall be selected by mutual agreement of the parties or, failing such agreement, shall be selected according to the aforesaid AAA rules. The parties shall bear the costs of arbitration equally unless the arbitrators, pursuant to their right, but not their obligation, require the non-prevailing party to bear all or any unequal portion of the prevailing party's costs. The decision by the arbitrators shall be made within ninety (90) days after the selection of the arbitrators. The decision of the arbitrators shall be final and may be sued on or enforced by the party in whose favor it decides in any court of competent jurisdiction at the option of such party. The arbitrators will be instructed to prepare and deliver a written, reasoned opinion conferring their decision. The rights and obligations of the parties to arbitrate any dispute relating to the interpretation or performance of this Agreement or the grounds for the termination thereof shall survive the expiration or termination of this Agreement for any reason.

9.4 FORCE MAJEURE. Neither party shall be held liable or responsible to the other party nor shall either party be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement (other than payment of monies due) when such failure or delay is caused by or results from causes beyond reasonable control of the affected party including but not limited to fire, floods, embargoes, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances, acts of God or acts, omissions or delays in acting by any governmental authority, or earthquakes, provided that the affected party uses reasonable efforts to overcome such failure or delay.

9.5 ASSIGNMENT. This Agreement may not be assigned or otherwise transferred, nor, except as expressly provided hereunder, may any rights or obligations hereunder be assigned or transferred, by either party without the written consent of the other party; provided, however, that either party may, without such consent, assign this Agreement and its rights and obligations hereunder (a) in connection with the transfer or sale of all or substantially all of its business, if such assets include substantially all of the assets relating to its performance of its obligations hereunder, (b) to a wholly owned subsidiary or, (c) in the event of its merger or consolidation with another company at any time during the term of this Agreement. Any purported assignment in violation of this Section 9.5 shall be void. Any permitted assignee shall assume all obligations of its assignor under this Agreement.

9.6 PUBLICITY. The parties agree that neither party will originate any news release or other public announcement, written or oral, or otherwise make any disclosure relating to the existence or terms of or performance under this Agreement without the prior written approval of the other party, except as may otherwise be required by law, or as provided in Section 7.4.

9.7 EXPORT LAWS. Each party hereby agrees that no technology or information licensed from the other, and no product thereof, will be made available or re-exported, directly or indirectly, except in compliance with

all applicable export laws and regulations.

9.8 SEVERABILITY. Both parties hereby expressly agree and contract that it is the intention of neither party to violate any laws, rules, regulations, treaty or decision of any

government agency or executive body thereof of any country or community or association of countries. Should a court or governmental authority of competent jurisdiction determine that one or more provisions of this Agreement are invalid or unenforceable by reason of such a violation, then the parties hereto shall attempt to substitute, by mutual consent, valid provisions for such invalid provisions, which valid provisions closely approximate the economic effect of the invalid provisions. If the parties are unable to formulate a mutually acceptable provision to replace any invalid provision, then such invalid provisions shall be severed from this Agreement and the invalidity of such provision shall not affect the validity of the Agreement as a whole.

9.9 NOTICES. Any notice or report required or permitted to be given or made under this Agreement by one of the parties hereto to the other shall be in writing, delivered personally or by facsimile (and promptly confirmed by telephone, personal delivery or courier) or courier, postage prepaid, addressed to such other party at its address indicated on the first page of this Agreement (to the attention of Gary Lyons, if to Neurocrine, and to the attention of James Gower, if to Rigel), or to such other address as the addressee shall have last furnished in writing to the address or and shall be effective upon receipt by the addressee.

9.10 APPLICABLE LAW. This Agreement shall be governed by and construed in accordance with the laws of the State of California, without regard to its choice of law provisions, and any applicable laws of the United States.

9.11 ENTIRE AGREEMENT; AMENDMENT. This Agreement contains the entire understanding of the parties with respect to the subject matter hereof. All express or implied agreements and understandings, either oral or written, heretofore made are expressly merged into and made a part of this Agreement. This Agreement may be amended, or any term hereof modified, only by a written instrument duly executed by both parties hereto.

9.12 INDEPENDENT CONTRACTORS. It is expressly agreed that Neurocrine and Rigel shall be independent contractors and that the relationship between the two parties shall not constitute a partnership, joint venture or agency of any kind. Neither party shall have the authority to make any statements, representations or commitments of any kind, or to take any action, which shall be binding on the other, without the prior written authorization of the other party to do so.

9.13 WAIVER. The waiver by either party hereto of any right hereunder or the failure to perform or of a breach by the other party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by said other party whether of a similar nature or otherwise.

9.14 COUNTERPARTS. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the parties hereto have duly executed this Collaborative Agreement.

NEUROCRINE, INC.	RIGEL, INC.
By: /s/ Kevin C. Gorman	By: /s/ James Gower
Kevin C. Gorman	James Gower
Title: Senior Director, Business Development	Title: Chief Executive Officer

Exhibit 10.11

RIGEL PHARMACEUTICALS
24 WINDSOR DRIVE, HILLSBOROUGH. CA 94010
PHONE/FAX: 415-579-4638

January 16, 1997

Dr. Donald G. Payan
24 Windsor Drive
Hillsborough, CA 94010

RE: EMPLOYMENT AGREEMENT

Dear Don:

Rigel Pharmaceuticals, Inc. (the "Company") is pleased to offer you the position of Vice President Research and Chief Operating Officer of the Company beginning January 16, 1997 ("Effective Date") on the terms set forth below (the "Agreement").

As Vice President Research and COO, you will perform the duties customarily associated with this position, and such duties as may be assigned to you by the Company's President and CEO. Of course, the Company may change your position, duties and work location from time to time, as it deems necessary.

Your annual salary will be $185,000 ("Base Salary"), less standard deductions and withholdings, paid semi-monthly. You will be expected to work as required to complete your job duties.

In addition, upon formal approval by the Board, the Company will issue to you 750,000 shares of Company founders common stock as described in the Company's Stock Purchase Agreement (the "Founders Stock"). This Founders Stock will be subject to the repuchase provisions contained in the Stock Purchase Agreement (the "Purchase Option"). If your employment with the Company is terminated without cause within three years, then the Founders Stock which remains subject to the Purchase Option will immediately lapse according to the following: (i) in the event at least one-third (1/3) of the Founders Stock remains subject to the Purchase Option, then the Purchase Option shall lapse with respect to one-third (1/3) of the Founders Stock; or (ii) in the event less than one-third (1/3) of the Founders Stock remains subject to the Purchase Option, then the Purchase Option shall lapse with respect to all such Founders Stock.

In addition to your salary and equity compensation, on the Effective Date the Company will provide you with sick and vacation leave, medical and dental insurance coverage, and any other benefits consistent with Company policy for exempt, full-time employees. Details about these benefits are available for your review. The Company reserves the right to modify your compensation and benefits from time to time, as it deems necessary.

The Company agrees to reimburse you for reasonable documented business expenses pursuant to Company policy.

You will be expected to abide by all of the Company's policies and procedures. As a condition of your employment, you also agree to sign and comply with the Company's Proprietary Information and Inventions Agreement (attached hereto as Exhibit A).

By accepting this offer, you represent and warrant that you are not a parry to any agreement with any third party or prior employer which would conflict with or inhibit your performance of your duties with the Company.

Either you or the Company may terminate your employment relationship at any time for any reason whatsoever, with or without cause or advance notice. This at-will employment relationship cannot be changed except in a writing signed by a duly authorized officer of the Company. If the Company terminates your employment without cause, the Company will make severance payments to you in the form of continuation of your base salary in effect on the Effective Date for one (1) year following your separation from the Company. These payments will be made on the Company's ordinary payroll dates, and will be subject to standard payroll deductions and withholdings. In the event of such termination, you will not be entitled to any additional compensation or benefits beyond what is provided in this paragraph and in the paragraph above relating to acceleration of Founders Stock vesting. If you resign or your employment is terminated for cause, all compensation and benefits will cease

immediately, and you will receive no severance benefits. For purposes of this Agreement, "cause" shall mean misconduct, including: (i) conviction of any felony or any crime involving moral turpitude or dishonesty; (ii) participation in a fraud or act of dishonesty against the Company; (iii) material breach of the Company's policies; (iv) damage to the Company's property; (v) material breach of this Agreement or your Proprietary Information and Inventions Agreement; or (vi) conduct by you which in the good faith and reasonable determination of the Board demonstrate s gross unfitness to serve.

You agree that, for one (1) year following the termination of your employment with the Company, you will not personally initiate or participate in the solicitation of any employee of the Company or any of its affiliates to terminate his or her relationship with the Company or any of its affiliates in order to become an employee for any other person or business entity.

To ensure rapid and economical resolution of any disputes which may arise under this Agreement, you and the Company agree that any and all disputes or controversies, whether of law or fact of any nature whatsoever (including, but not limited to, all state and federal statutory and discrimination claims), with the sole exception of those dispute, which may arise from your Proprietary Information and inventions Agreement, arising from or regarding your employment

or the termination thereof, or the interpretation, performance, enforcement or breach of this Agreement shall be resolved by confidential, final and binding arbitration under the then-existing Rules of Practice and Procedure of Judicial Arbitration and Mediation Services, Inc., which shall be conducted in San Francisco, California.

This Agreement, including Exhibit A constitutes the complete, final and exclusive embodiment of the entire agreement between you and the Company with respect to the terms and conditions of your employment. This Agreement is entered into without reliance upon any promise, warranty or representation, written or oral, other than those expressly contained herein, and it supersedes any other such promises, warranties, representations or agreements. It may not be amended or modified except by a written instrument signed by you and a duly authorized officer of the Company. If any provision of this Agreement is determined to be invalid or unenforceable, in whole or in part, this determination will not affect any other provision of this Agreement. This Agreement shall be construed and interpreted in accordance with the laws of the State of California and shall be deemed drafted by both parties.

As required by law, this offer of employment is subject to satisfactory proof of your right to work in the United States.

If you choose to accept our offer under the terms described above, please sign below and return this letter to me.

We look forward to a productive and enjoyable work relationship.

Very truly yours,

RIGEL PHARMACEUTICALS, INC.

By: /s/James M. Gower

James M. Gower

ACCEPTED BY: /s/Donald G. Payan

Donald G. Payan

DATE: 1/16/97

EXHIBIT 10.12

BUILD-TO-SUIT LEASE

Landlord: Britannia Pointe Grand Limited Partnership

Tenant: Rigel, Inc.

Date: June 2, 1998

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BUILD-TO-SUIT LEASE

THIS BUILD-TO-SUIT LEASE ("LEASE") is made and entered into as of June 2, 1998, by and between BRITANNIA POINTE GRAND LIMITED PARTNERSHIP, a Delaware limited partnership ("LANDLORD"), and RIGEL, INC., a Delaware corporation ("TENANT").

THE PARTIES AGREE AS FOLLOWS:

1. PROPERTY

1.1 LEASE OF PROPERTY.

(a) Landlord leases to Tenant and Tenant hires and leases from Landlord, on the terms, covenants and conditions hereinafter set forth, the building (the "BUILDING") to be constructed pursuant to Article 5 hereof and EXHIBIT C attached hereto on a portion of the real property described in EXHIBIT A attached hereto (the "PROPERTY"), to consist of a two-story office and laboratory building containing approximately 60,964 square feet. The location of the Building on the Property is intended to be substantially as shown on the site plan attached hereto as EXHIBIT B (the "SITE PLAN"). The Property is part of the Britannia Pointe Grand Business Park (the "CENTER") on East Grand Avenue in the City of South San Francisco, County of San Mateo, State of California, which presently consists of the Property and certain adjacent undeveloped land and presently includes the existing buildings designated as Buildings D, E, F and G on the Site Plan (containing, in the aggregate, approximately 177,253 square feet of office and research and development space), as well as one additional building of approximately 47,000 square feet presently under construction in the area designated "MetaXen Building" on the Site Plan. The Building and the other improvements to be constructed on the Property pursuant to Article 5 hereof and EXHIBIT C attached hereto are sometimes referred to collectively herein as the "IMPROVEMENTS." The parking areas, driveways, sidewalks, landscaped areas and other portions of the Center that lie outside the exterior walls of the buildings now existing or to be constructed in the Center, as depicted in the Site Plan and as hereafter modified by Landlord from time to time in accordance with the provisions of this Lease, are sometimes referred to herein as the "COMMON AREAS."

(b) As an appurtenance to Tenant's leasing of the Building pursuant to Section 1. l(a), Landlord hereby grants to Tenant, for the benefit of Tenant and its employees, suppliers, shippers, customers and invitees, during the term of this Lease, the non-exclusive right to use, in common with others entitled to such use, (i) those portions of the Common Areas improved from time to time for use as parking areas, driveways, sidewalks, landscaped areas, or for other common purposes, and (ii) all access easements and similar rights and privileges relating to or appurtenant to the Center and created or existing from time to time under any access easement agreements, declarations of covenants, conditions and restrictions, or other written agreements now or hereafter of record with respect to the Center, subject however to any limitations applicable to such rights and privileges under applicable law, under this Lease and/or under the written agreements creating such rights and privileges.

1.2 LANDLORD'S RESERVED RIGHTS. To the extent reasonably necessary to permit Landlord to exercise any rights of Landlord and discharge any obligations of Landlord under this Lease, Landlord shall have, in addition to the right of entry set forth in Section 16.1 hereof, the following rights: (i) to make changes to the Common Areas, including, without limitation, changes in the location, size or shape of any portion of the Common Areas, and to relocate parking spaces in the Center (but not materially decrease the number of such parking spaces in areas of the Center generally adjacent to the Building); (ii) to close temporarily any of the Common Areas for maintenance or other reasonable purposes, provided that reasonable parking and reasonable access to the Building remain available;

(iii) to construct, alter or add to other buildings and Common Area improvements in the center (including, but not limited to, construction of site improvements, buildings and Common Area improvements in adjacent portions of the Center as it may exist from time to time); (iv) to build in areas adjacent to the Center and to add such areas to the Center; (v) to use the Common Areas while engaged in making additional improvements, repairs or alterations to the Center Or any portion thereof; and (vi) to do and perform such other acts with respect to the Common Areas and the Center as may be necessary or appropriate; PROVIDED, however, that notwithstanding anything to the contrary in this Section 1.2, Landlord's exercise of its rights hereunder shall not cause any material diminution of Tenant's rights, nor any material increase of Tenant's obligations, under this Lease or with respect to the

Improvements.

2. TERM

2.1 TERM. The term of this Lease shall commence upon mutual execution of this Lease by Landlord and Tenant. Tenant's minimum rental and Operating Expense obligations shall commence on the earlier of (i) the date which is six (6) months after the date Landlord delivers to Tenant a Structural Completion Certificate pursuant to the Workletter attached hereto as EXHIBIT C (subject to any adjustments authorized or required under the provisions of such EXHIBIT C), correctly notifying Tenant that Landlord's construction of the shell of the Building pursuant to Article V and EXHIBIT C is substantially complete, or (ii) the date Tenant takes occupancy of and commences operation of its business in the Building, the earlier of such dates being herein called the "RENT COMMENCEMENT DATE," and shall end on the day (the "TERMINATION DATE") immediately preceding the date seventeen (17) years thereafter, unless sooner terminated or extended (if applicable) as hereinafter provided.

2.2 EARLY POSSESSION. Tenant shall have the nonexclusive right to occupy and take possession of the Building from and after the date of Landlord's delivery of the Structural Completion Certificate described in clause (i) of Section 2.1, even though Landlord will be continuing to construct the balance of Landlord's Work as contemplated in EXHIBIT C, for the purpose of constructing Tenant's Work as contemplated in EXHIBIT C and for the purpose of installing fixtures and furniture, laboratory equipment, computer equipment, telephone equipment, low voltage data wiring and personal property and other similar work related to the construction of Tenant's Work and/or preparatory to the commencement of Tenant's business on the Property. Such occupancy and possession, and any early access under the next sentence of this Section 2.2, shall be subject to and upon all of the terms and conditions of this Lease and of the Workletter attached hereto as EXHIBIT C including, but not limited to, conditions relating to the maintenance of required insurance), except that Tenant shall have no obligation to pay minimum rental or Operating Expenses for any period prior to the Rent Commencement Date as determined under Section 2.1; such early possession shall not advance or otherwise affect the Rent Commencement Date or Termination Date determined under Section 2.1. Tenant shall also be entitled to have early access to the Property at all appropriate times prior to Landlord's delivery of the Structural Completion Certificate, subject to the approval of Landlord and its general contractor (which approval shall not be unreasonably withheld or delayed) and to all other provisions of this Section 2.2, solely for the purpose of performing work preparatory to the construction of Tenant's Work or necessary for the orderly sequencing of such work, and Tenant shall not be required to pay minimum rental or Operating Expenses by reason of such early access until the Rent Commencement Date otherwise occurs; without limiting the generality of the preceding portion of this sentence, Tenant shall be entitled to have early access to the Property and the Building as soon as the roof metal decking is in place to begin hanging electrical, mechanical and plumbing services from the overhead structure, subject to all of the provisions of this Section 2.2. Tenant shall not interfere with or delay Landlord's contractors by any early access, occupancy or possession under this Section 2.2, shall coordinate and cooperate with Landlord and its contractors (who shall similarly coordinate and cooperate with Tenant and its contractors) to minimize any interference or delay by either party with respect to the other party's work following Landlord's delivery of the Structural Completion Certificate, and shall indemnify, defend and hold harmless Landlord and its agents and employees from and against any and all claims, demands, liabilities, actions, losses, costs and expenses, including

(but not limited to) reasonable attorneys' fees, arising out of or in connection with Tenant's early entry upon the Property hereunder.

2.3 DELAY IN POSSESSION. Landlord agrees to use its best reasonable efforts to complete its portion of the work described in Section 5.1 and EXHIBIT C promptly, diligently and within the respective time periods set forth in the Estimated Construction Schedule attached hereto as EXHIBIT D and incorporated herein by this reference, as such schedule may be modified from time to time by mutual written agreement of Landlord and Tenant, and subject to the effects of any delays caused by or attributable to Tenant or any other circumstances beyond Landlord's reasonable control (excluding financial inability); PROVIDED, however, that except to the extent caused by a material default by Landlord of its obligations set forth in this Lease (including, but not- limited to, its obligations set forth in this Section 2.3 and in Section 5.1 and EXHIBIT C), Landlord shall not be liable for any damages caused by any delay in the completion of such work, nor shall any such delay affect the validity of this Lease or the obligations of Tenant hereunder. Notwithstanding any other provision of this Section 2.3, however, if Landlord fails to deliver the Structural Completion Certificate and tender possession of the completed structural portions of the Building Shell (I.E., those portions required to be completed as a condition of delivery of the

Structural Completion Certificate) to Tenant by the date which is twenty-one (21) months after the date of this Lease, then Tenant shall have the right to terminate this Lease without further liability hereunder by written notice delivered to Landlord at any time prior to Landlord's delivery of the Structural Completion Certificate and tender of possession of the completed structural portions of the Building Shell to Tenant; PROVIDED, however, that the 21-month period set forth in this sentence shall be extended, day for day, for a period equal to the length of any delays in Landlord's design and construction of the Building Shell that are caused by any material default by Tenant in the performance of its obligations under this Lease, including (but not limited to) any failure of Tenant to make prompt and timely delivery to Landlord of all information reasonably necessary for Landlord to complete the preparation of all drawings, designs and specifications for the Building Shell and/or any failure of Tenant to respond in a prompt and timely manner to any requests by Landlord or its architect for approval of drawings, designs, specifications, changes or other matters requiring Tenant's review or approval under the provisions of EXHIBIT C.

2.4 ACKNOWLEDGEMENT OF RENT COMMENCEMENT. Promptly following the Rent Commencement Date, Landlord and Tenant shall execute a written acknowledgement of the Rent Commencement Date, Termination Date and related matters, substantially in the form attached hereto as EXHIBIT E (with appropriate insertions), which acknowledgement shall be deemed to be incorporated herein by this reference. Notwithstanding the foregoing requirement, the failure of either party to execute such a written acknowledgement shall not affect the determination of the Rent Commencement Date, Termination Date and related matters in accordance with the provisions of this Lease.

2.5 HOLDING OVER. If Tenant holds possession of the Property or any portion thereof after the term of this Lease WITH Landlord's written consent, then except as otherwise specified in such consent, Tenant shall become a tenant from month to month at one hundred ten percent (110%) of the rental and otherwise upon the terms herein specified for the period immediately prior to such holding over and shall continue in such status until the tenancy is terminated by either party upon not less than thirty (30) days prior written notice. If Tenant holds possession of the Property or any portion thereof after the term of this Lease WITHOUT Landlord's written consent, then Landlord in its sole discretion may elect (by written notice to Tenant) to have Tenant become a tenant either from month to month or at will at one hundred fifty percent (150%) of the rental (prorated on a daily basis for an at-will tenancy, if applicable) and otherwise upon the terms herein specified for the period immediately prior to such holding over, or may elect to pursue any and all legal remedies available to Landlord under applicable law with respect to such unconsented holding over by Tenant. Tenant shall indemnify and hold Landlord harmless from any loss, damage, claim, liability, cost or expense (including reasonable attorneys' fees) resulting from any delay by Tenant in surrendering the Property or any portion thereof (except to the extent such delay is with Landlord's prior written consent), including but not limited to any claims made by a

succeeding tenant by reason of such delay. Acceptance of rent by Landlord following expiration or termination of this Lease shall not constitute a renewal of this Lease.

2.6 OPTION TO EXTEND TERM. Tenant shall have the option to extend the term of this Lease, at the minimum rental set forth in Section 3. l(b) and (c) and otherwise upon all the terms and provisions set forth herein with respect to the initial term of this Lease, for up to two (2) additional periods of five (5) years each, the first commencing upon the expiration of the initial term hereof and the second commencing upon the expiration of the first extended term, if any. Exercise of such option with respect to the first such extended term shall be by written notice to Landlord at least nine (9) months prior to the expiration of the initial term hereof; exercise of such option with respect to the second extended term, if the first extension option has been duly exercised, shall be by like written notice to Landlord at least nine (9) months prior to the expiration of the first extended term hereof. If Tenant is in default hereunder, beyond any applicable notice and cure periods, on the date of such notice or on the date any extended term is to commence, then the exercise of the option shall be of no force or effect, the extended term shall not commence and this Lease shall expire at the end of the then current term hereof (or at such earlier time as Landlord may elect pursuant to the default provisions of this Lease). If Tenant properly exercises one or more extension options under this Section, then all references in this Lease (other than in this Section 2.6) to the "term" of this Lease shall be construed to include the extension term(s) thus elected by Tenant. Except as expressly set forth in this Section 2.6, Tenant shall have no right to extend the term of this Lease beyond its prescribed-term.

3. RENTAL

3.1 MINIMUM RENTAL.

(a) RENTAL AMOUNTS. Tenant shall pay to Landlord as minimum rental for the Building, in advance, without deduction, offset, notice or demand, on or before the Rent Commencement Date and on or before the first day of each subsequent calendar month of the term of this Lease, the following amounts per month, subject to adjustment in accordance with the terms of this Section 3.1:

<TABLE>
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MONTHS	MONTHLY MINIMUM RENTAL	
<S>	<C>	
001 - 012	$ 121,928	($2.00/sq ft)
013 - 024	121,928	($2.00/sq ft)
025 - 036	177,405	($2.91/sq ft)
037 - 048	190,817	($3.13/sq ft)
049 - 060	195,085	($3.20/sq ft)
061 - 072	196,304	($3.22/sq ft)
073 - 084	200,572	($3.29/sq It)
085 - 096	165,822	($2.72/sq ft)
097 - 108	170,699	($2.80/sq ft)
109 - 120	175,576	($2.88/sq ft)
121 - 132	158,506	($2.60/sq ft)
133 - 144	163,993	($2.69/sq ft)
145 - 156	170,090	($2.79/sq ft)
157 - 168	176,186	($2.89/sq ft)
169 - 180	162,164	($2.66/sq ft)
181 - 192	168,261	($2.76/sq ft)
193 - 204	174,967	($2.87/sq ft)

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If the obligation to pay minimum rental hereunder commences on other than the first day of a calendar month or if the term of this Lease terminates on other than the last day of a calendar month, the minimum rental for such first or last month of the term of this Lease, as the case may be, shall be prorated based on the number of days the term of this Lease is in effect during such month. If an increase in minimum rental becomes effective on a day other

than the first day of a calendar month, the minimum rental for that month shall be the sum of the two applicable rates, each prorated for the portion of the month during which such rate is in effect.

(b) RENTAL AMOUNTS DURING FIRST EXTENDED TERM. If Tenant properly exercises its right to extend the term of this Lease pursuant to Section 2.6 hereof, the minimum rental during the first extended term shall be equal to ninety-five percent (95 %) of the fair market rental value of the Building (as defined below), including any rental increase provisions then customary in the City of South San Francisco for comparable commercial leases for office, laboratory and research and development projects, determined as of the commencement of such extended term in accordance with this paragraph. Upon Landlord's receipt of a proper notice of Tenant's exercise of its option to extend the term of this Lease, the parties shall have sixty (60) days in which to agree on the fair market rental (including any applicable rental increase provisions) for the Building at the commencement of the first extended term for the uses permitted hereunder. If the parties agree on such fair market rental and rental increase provisions (if any), they shall execute an amendment to this Lease stating the amount of the applicable minimum monthly rental and any applicable rental increase provisions. If the parties are unable to agree on such rental (including an), applicable rental increase provisions) within such sixty (60) day period, then within fifteen (15) days after the expiration of such period each party, at its cost and by giving notice to the other party, shall appoint a real estate appraiser with at least five (5) years experience appraising similar commercial properties in northeastern San Mateo County to appraise and set the fair market rental and any applicable rental increase provisions for the Building at the commencement of the first extended term in accordance with the provisions of this Section 3.1(b). If either party fails to appoint an appraiser within the allotted time, the single appraiser appointed by the other party shall be the sole appraiser. If an appraiser is appointed by each party and the two appraisers so appointed are unable to agree upon a fair market rental (and any appropriate rental increase provisions) within thirty (30) days after the appointment of the second, the two appraisers shall appoint a third similarly qualified appraiser within ten (10) days after expiration of such 30-day period; if they are unable to agree upon a third appraiser, then either party may, upon not less than five (5) days notice to the other party, apply to the Presiding Judge of the San Mateo County Superior Court for the appointment of a third qualified appraiser. Each party shall bear its own legal fees in connection with appointment of the third appraiser and shall bear one-half of any other costs of appointment of the third appraiser and of such third

appraiser's fee. The third appraiser, however selected, shall be a person who has not previously acted for either party in any capacity. Within thirty (30) days after the appointment of the third appraiser, a majority of the three appraisers shall set the fair market rental and any applicable rental increase provisions for the first extended term and shall so notify the parties. If a majority are unable to agree within the allotted time, (i) the three appraised fair market rentals shall be added together and divided by three and the resulting quotient shall be the fair market rental for the first extended term, and (ii) the applicable rental increase provision shall be equal to the mathematical average (or the nearest reasonable approximation thereto) of the two rental increase provisions that are most closely comparable, which determinations shall be binding on the parties and shall be enforceable in any further proceedings relating to this Lease. For purposes of this Section 3.1(b), the "FAIR MARKET RENTAL" of the Building shall be determined with reference to the then prevailing market rental rates for properties in the City of South San Francisco with shell and standard office, research and development improvements and site (common area) improvements comparable to those then existing in the Building and on the Property; no equipment or laboratory improvements constructed by or for Tenant, whether at Landlord's or Tenant's expense and whether paid for in cash or through additional rent or financed in any other manner (including, but not limited to, equipment and laboratory improvements installed as part of the initial tenant improvements pursuant to Section 5.1 and EXHIBIT C), shall be taken into account in determining such fair market rental.

(c) RENTAL AMOUNTS DURING SECOND EXTENDED TERM. If Tenant properly exercises its right to a second extended term of this Lease pursuant to Section 2.6 hereof, the minimum rental during such second extended term shall be determined in the same manner provided in the preceding paragraph for the first extended term, except that the determination shall be made as of the commencement of the second extended term.

(d) RENTAL ADJUSTMENT DUE TO CHANGE IN SQUARE FOOTAGE. The minimum rental amounts specified in this Section 3.1 are based upon an estimated area of 60,964 square feet for the Building. If the actual area of the Building (measured from the exterior faces of exterior wails and from the dripline of any overhangs, except that in the case of any two-story recesses or overhangs, the area to the dripline of the overhang shall be counted as part of the area of the first story but not as part of the area of the second story), when completed, is greater or less than such estimated area, then the minimum rentals specified in Section 3. l(a) shall be adjusted for each rental period in strict proportion to the ratio between the actual area of the Building during the applicable period (determined on the basis of measurement described above in this sentence) and the assumed area of 60,964 square feet. Measurement of building area under this paragraph shall be made initially by Landlord's architect, subject to review and approval by Tenant's architect.

3.2 LATE CHARGE. If Tenant fails to pay when due rental or other amounts due Landlord hereunder, such unpaid amounts shall bear interest for the benefit of Landlord at a rate equal to the lesser of fifteen percent (15%) per annum or the maximum rate permitted by law, from the date due to the date of payment. In addition to such interest, Tenant shall pay to Landlord a late charge in an amount equal to six percent (6%) Of any installment of minimum rental and any other amounts due Landlord if not paid in full on or before the fifth (5th) day after such rental or other amount is due. Tenant acknowledges that late payment by Tenant to Landlord of rental or other amounts due hereunder will cause Landlord to incur costs not contemplated by this Lease, including, without limitation, processing and accounting charges and late charges which may be imposed on Landlord by the terms of any loan relating to the Property. Tenant further acknowledges that it is extremely difficult and impractical to fix the exact amount of such costs and that the late charge set forth in this Section 3.2 represents a fair and reasonable estimate thereof. Acceptance of any late charge by Landlord shall not constitute a waiver of Tenant's default with respect to overdue rental or other amounts, nor shall such acceptance prevent Landlord from exercising any other rights and remedies available to it. Acceptance of rent or other payments by Landlord shall not constitute a waiver of late charges or interest accrued with respect to such rent or other payments or any prior installments thereof, nor of any other defaults by Tenant, whether monetary or non-monetary in nature, remaining uncured at the time of such acceptance of rent or other payments.

4. STOCK WARRANTS

4.1 STOCK WARRANTS. Within thirty (30) days after the execution of this Lease, as a condition to Landlord's obligations hereunder, Tenant shall deliver to Landlord or Landlord's designees (which may be any partners, shareholders or affiliates of Landlord or any affiliates of any such partners, shareholders or affiliates of Landlord) warrants registered in the name of Landlord or Landlord's designees for the acquisition of an aggregate of one hundred fifty thousand (150,000) shares of Tenant's common stock,

which warrants shall be in form and substance mutually satisfactory to Landlord and Tenant. The warrants shall have an exercise price consistent with the most recent arm's-length financing consummated by Tenant at the time of execution of this Lease and shall be exercisable for a period beginning on the date of this Lease and ending on the seventh (7th) anniversary of the closing of the initial public offering (if any) of Tenant's common stock.

5. CONSTRUCTION

5.1 CONSTRUCTION OF IMPROVEMENTS.

(a) Landlord shall, at Landlord's cost and expense (except as otherwise provided herein and in EXHIBIT C), construct Landlord's Work as defined in and in accordance with the terms and conditions of the Workletter attached hereto as EXHIBIT C (the "WORKLETTER"). Landlord shall use its best reasonable efforts to complete such construction promptly, diligently and within the applicable time periods set forth in the Estimated Construction Schedule attached hereto as EXHIBIT D and incorporated herein by this

reference, as such schedule may be modified from time to time in accordance with the Workletter, subject to the effects of any delays caused by Tenant or any other circumstances beyond Landlord's reasonable control (excluding any financial inability), and subject to the provisions of Section 2.3 above.

(b) Tenant shall, at Tenant's cost and expense (except as otherwise provided herein and in EXHIBIT C), promptly and diligently construct Tenant's Work as defined in and in accordance with the terms and conditions of the Workletter.

5.2 CONDITION OF PROPERTY. Landlord shall deliver the Building Shell and other Improvements constructed by Landlord to Tenant clean and free of debris, promptly upon completion of construction thereof, and Landlord warrants to Tenant that the Building Shell and other Improvements constructed by Landlord (i) shall be free from material structural defects and shall be in good operating condition on the Rent Commencement Date, and (ii) shall be constructed in compliance in all material respects with the plans and specifications developed pursuant to the Workletter and mutually approved (to the extent required thereunder) by Landlord and Tenant, subject to any changes implemented in such specifications in accordance with the procedures set forth in the Workletter. If this warranty is violated in any respect, then it shall be the obligation of Landlord, after receipt of written notice from Tenant setting forth with specificity the nature of the violation, to promptly, :it Landlord's sole cost, correct the condition(s) constituting such violation. Tenant's failure to give such written notice to Landlord within one hundred eighty (180) days after the Commencement Date shall give rise to a conclusive presumption that Landlord has complied with all Landlord's obligations hereunder, except with respect to latent defects (as to which such 180-day limitation shall not apply). Without limiting the scope of Landlord's obligations under the foregoing provisions of this Section 5.2, Landlord also agrees to either (x) use its best reasonable efforts to enforce when and as necessary, for the benefit of Tenant and the Improvements, any and all contractor's and/or manufacturer's warranties extending more than one hundred eighty (180) days after the Rent Commencement Date with respect to any of Landlord's Work or, at Tenant's request, (y) assign any or all of such warranties to Tenant for enforcement purposes (PROVIDED, however, that Landlord may reserve joint enforcement rights under such warranties to the extent of Landlord's continuing obligations or warranties hereunder). TENANT ACKNOWLEDGES THAT THE WARRANTY CONTAINED IN THIS SECTION IS IN LIEU OF ALL OTHER WARRANTIES, EXPRESS OR IMPLIED, WITH RESPECT TO THE PHYSICAL CONDITION OF THE IMPROVEMENTS TO BE CONSTRUCTED BY LANDLORD AND THAT LANDLORD MAKES NO OTHER WARRANTIES EXCEPT AS EXPRESSLY SET FORTH IN THIS LEASE.

5.3 COMPLIANCE WITH LAW. Landlord warrants to Tenant that the Building Shell and other Improvements constructed by Landlord (when constructed), as they exist on the Rent Commencement Date, but without regard to the use for which Tenant will occupy the Building, shall not violate any covenants or restrictions of record or any applicable law, building code, regulation or ordinance in effect on the Rent Commencement Date. Tenant warrants to Landlord that the Tenant Improvements and any other improvements constructed by Tenant from time to time shall not violate any applicable law, building code, regulation or ordinance in effect on the Rent Commencement Date or at the time such improvements are placed in service. If it is determined that any of these warranties has been violated, then it shall be the obligation of the warranting party, after written notice from the other party, to correct the condition(s) constituting such violation promptly, at the warranting party's sole cost and expense. Tenant acknowledges that except as expressly set forth in this Lease, neither Landlord nor any agent of Landlord has made any representation or warranty as to the present or future suitability of the Property or Improvements for the conduct of Tenant's business or proposed business thereon.

6. TAXES

6.1 PERSONAL PROPERTY. Tenant shall be responsible for and shall pay prior to delinquency all taxes and assessments levied against or by reason of (a) any and all

alterations, additions and items installed or placed on or in the Building and taxed as personal property rather than as real property, and/or (b) all personal property, trade fixtures and other property placed by Tenant on or about the Property. Upon request by Landlord, Tenant shall furnish Landlord with satisfactory evidence of Tenant's payment thereof. If at any time during the term of this Lease any of said alterations, additions or personal property, whether or not belonging to Tenant, shall be taxed or assessed as part of the Center, then such tax or assessment shall be paid by Tenant to Landlord within fifteen (15) days after presentation by Landlord of copies of the tax bills in which such taxes and assessments are included and shall, for the purposes of this Lease, be deemed to be personal property taxes or assessments under this Section 6.1.

6.2 REAL PROPERTY. To the extent any real property taxes and assessments on the Property (including, but not limited to, the Improvements) are assessed directly to Tenant, Tenant shall be responsible for and shall pay prior to delinquency all such taxes and assessments levied against the Property. Upon request by Landlord, Tenant shall furnish Landlord with satisfactory evidence of Tenant's payment thereof. To the extent the Property and/or Improvements are taxed or assessed to Landlord following the Rent Commencement Date, such real property taxes and assessments shall constitute Operating Expenses (as that term is defined in Section 7.2 of this Lease) and shall be paid in accordance with the provisions of Article 7 of this Lease.

7. OPERATING EXPENSES

7.1 PAYMENT OF OPERATING EXPENSES.

(a) Tenant shall pay to Landlord, at the time and in the manner hereinafter set forth, as additional rental, an amount equal to fifteen and fifty-seven hundredths percent (15.57 %) ("TENANT'S OPERATING COST SHARE") of the Operating Expenses defined in Section 7.2.

(b) Tenant's Operating Cost Share as specified in paragraph (a) of this Section is based upon an estimated area of 60,964 square feet for the Building and upon an aggregate area of 391,585 square feet for the existing buildings owned by Landlord in the Center (Buildings D, E, F and G as shown on the Site Plan), the Building and the two additional buildings that Landlord is committed to build in the Center (the MetaXen Building and the SUGEN Building, as designated on the Site Plan). If the actual area of the Building (when completed) or of the other buildings owned from time to time by Landlord in the Center, as determined in good faith by Landlord's architect on the basis of measurement set forth in Section 3.1 (d) hereof, differs from the assumed numbers set forth above (including, but not limited to, any such difference arising from the MetaXen Building and/or the SUGEN Building being completed and occupied later than the Rent Commencement Date hereunder), then Tenant's Operating Cost Share shall be adjusted to reflect the actual areas so determined as they exist from time to time.

(c) If Landlord constructs additional buildings in the Center or on any adjacent property owned by Landlord and operated, for common area purposes, on an integrated basis with the Center, Tenant's Operating Cost Share shall be adjusted to be equal to the percentage determined by dividing the gross square footage of the Building as it then exists by the gross square footage of all buildings located in the Center or on any applicable adjacent property owned by Landlord as described above. In determining such percentage, a building shall be taken into account from and after the date on which a tenant first enters into possession of the building or a portion thereof, and the good faith determination of the gross square footage of any such building by Landlord's architects shall be final and binding upon the parties.

7.2 DEFINITION OF OPERATING EXPENSES.

(a) Subject to the exclusions and provisions hereinafter contained, the term "OPERATING EXPENSES" shall mean the total costs and expenses incurred by or allocable to

Landlord for management, operation and maintenance of the Improvements, the Property and the Center, including, without limitation, costs and expenses of (i) insurance (which may include, at Landlord's option, earthquake insurance as part of or in addition to any casualty or property insurance policy), property management, landscaping, and the operation, repair. and maintenance of buildings and Common Areas: (ii) all utilities and services; (iii) real

and personal property taxes and assessments or substitutes therefor levied or assessed against the Center or any part thereof, including (but not limited to) any possessory interest, use, business, license or other taxes or fees, any taxes imposed directly on rents or services, any assessments or charges for police or fire protection, housing, transit, open space, street or sidewalk construction or maintenance or other similar services from time to time by any governmental or quasi-governmental entity, and any other new taxes on landlords in addition to taxes now in effect; (iv) supplies, equipment, utilities and tools used in management, operation and maintenance of the Center; (v) capital improvements to the Property, the Improvements or the Center, amortized over a reasonable period, (aa) which reduce or will cause future reduction of other items of Operating Expenses for which Tenant is otherwise required to contribute or (bb) which are required by law, ordinance, regulation or order of any governmental authority or (cc) of which Tenant has use or which benefit Tenant; and (vi) any other costs (including, but not limited to, any parking or utilities fees or surcharges) allocable to or paid by Landlord, as owner of the Center or Improvements, pursuant to any applicable laws, ordinances, regulations or orders of any governmental or quasi-governmental authority or pursuant to the terms of any declarations of covenants, conditions and restrictions now or hereafter affecting the Center or over which Tenant has non-exclusive usage rights as contemplated in Section 1. l(b) hereof. Operating Expenses shall not include any costs attributable to the work for which Landlord is required to pay under Article 5 or EXHIBIT C, nor any costs attributable to the initial construction of buildings or Common Area improvements in the Center. The distinction between items of ordinary operating maintenance and repair and items of a capital nature shall be made in accordance with generally accepted accounting principles applied on a consistent basis or in accordance with tax accounting principles, as determined in good faith by Landlord's accountants.

(b) Notwithstanding anything to the contrary contained in this Lease, the following shall not be included within Operating Expenses:

(i) Costs of maintenance or repair of the roof membrane for any building within the Center, except during periods (if any) in which costs of maintenance or repair of the roof membrane for the Building are likewise included as an Operating Expense (rather than being incurred directly by Tenant or passed through directly to Tenant on a building-by-building basis);

(ii) Leasing commissions, attorneys' fees, costs, disbursements, and other expenses incurred in connection with negotiations or disputes with tenants, or in connection with leasing, renovating or improving space for tenants or other occupants or prospective tenants or other occupants of the Center;

(iii) The cost of any service sold to any tenant (including Tenant) or other occupant for which Landlord is entitled to be reimbursed as an additional charge or rental over and above the basic rent and operating expenses payable under the lease with that tenant;

(iv) Any depreciation on the Building or on any other improvements in the Center;

(v) Expenses in connection with services or other benefits of a type that are not offered or made available to Tenant but that are provided to another tenant of the Center;

(vi) Costs incurred due to Landlord's violation of any terms or conditions of this Lease or of any other lease relating to the Building or to any other portion of the Center or the Property;

(vii) Overhead profit increments paid to any subsidiary or affiliate of Landlord for management or other services on or to the Center or any portion thereof or for supplies or other materials to the extent that the cost of the services, supplies or materials exceeds the cost that would have been paid had the services, supplies or materials been provided by unaffiliated parties on a competitive basis;

(viii) All interest, loan fees and other carrying costs related to any mortgage or deed of trust or related to any capital item, and all rental and other amounts payable under any ground or underlying lease, or under any lease for any equipment ordinarily considered to be of a capital nature (except (A) janitorial equipment which is not affixed to the Building and/or (B) equipment the cost of which, if purchased, would be considered an amortizable Operating Expense under the provisions of this Section 7.2, notwithstanding the capital nature of such equipment);

(ix) Any compensation paid to clerks, attendants or Other persons in commercial concessions operated by Landlord;

(x) Advertising and promotional expenditures;

(xi) Costs of repairs and other work occasioned by fire, windstorm or other casualty of an insurable nature, except to the extent of any applicable deductible amounts under insurance actually carried by Landlord;

(xii) Any costs, fines or penalties incurred due to violations by Landlord of any governmental rule or authority or of this Lease or any other lease of any portion of the Center or the Property, or due to Landlord's negligence or willful misconduct;

(xiii) Management costs to the extent they exceed a reasonable and competitive rate for such services in the market for management of comparable commercial properties in the San Francisco Bay Area;

(xiv) Costs for sculpture, paintings or other objects of art, and for any insurance thereon or extraordinary security in connection therewith;

(xv) Wages, salaries or other compensation paid to any executive employees above the grade of building manager;

(xvi) The cost of correcting any building code or other violations which were violations prior to the Rent Commencement Date;

(xvii) The cost of containing, removing or otherwise remediating any contamination of the Property (including the underlying land and groundwater) by any toxic or hazardous materials (including, without limitation, asbestos and PCBs); and

(xviii) Premiums for earthquake insurance coverage, but only to the extent (if any) that such premiums exceed, in any applicable period, a commercially reasonable rate, taking into account all relevant factors (including, but not limited to, the nature, size and location of the Center, the nature and value of the improvements therein that are owned by or insurable by Landlord, and the general availability and cost of commercial earthquake insurance in the insurance markets existing from time to time during the term of this Lease).

7.3 DETERMINATION OF OPERATING EXPENSES. On or before the Rent Commencement Date and during the last month of each calendar year of the term of this Lease ("LEASE YEAR"), or as soon thereafter as practical, Landlord shall provide Tenant notice of Landlord's estimate of the Operating Expenses for the ensuing Lease Year or applicable portion thereof. On or before the first day of each month during the ensuing Lease Year or applicable portion thereof, beginning on the Rent Commencement Date, Tenant shall pay to Landlord Tenant's Operating Cost Share of the portion of such estimated Operating Expenses allocable (on a prorata basis) to such month; PROVIDED, however, that if such notice is not given in the last

month of a Lease Year, Tenant shall continue to pay on the basis of the prior year's estimate, if any, until the month after such notice is given. If at any time or times it appears to Landlord that the actual Operating Expenses will vary from Landlord's estimate by more than five percent (5 %), Landlord may, by notice to Tenant, revise its estimate for such year and subsequent payments by Tenant for such year shall be based upon such revised estimate.

7.4 FINAL ACCOUNTING FOR LEASE YEAR.

(a) Within ninety (90) days after the close of each Lease Year, or as soon after such 90-day period as practicable, Landlord shall deliver to Tenant a statement of Tenant's Operating Cost Share of the Operating Expenses for such Lease Year prepared by Landlord from Landlord's books and records, which statement shall be final and binding on Landlord and Tenant (except as provided in Section 7.4(b)). If on the basis of such statement Tenant owes an amount that is more or less than the estimated payments for such Lease Year previously made by Tenant, Tenant or Landlord, as the case may be, shall pay the deficiency to the other party within thirty (30) days after delivery of the statement. Failure or inability of Landlord to deliver the annual statement within such ninety (90) day period shall not impair or constitute a waiver of Tenant's obligation to pay Operating Expenses, or cause Landlord to incur any liability for damages.

(b) At any time within three (3) months after receipt of Landlord's annual statement of Operating Expenses as contemplated in Section 7.4(a), Tenant shall be entitled, upon reasonable written notice to Landlord and during normal business hours at Landlord's office or such other places as Landlord shall designate, to inspect and examine those books and records of Landlord relating to the determination of Operating Expenses for the immediately preceding Lease Year covered by such annual statement or, if Tenant so elects by written notice to Landlord, to request an independent audit of such books and records. The independent audit of the books and

records shall be conducted by a certified public accountant acceptable to both Landlord and Tenant or, if the parties are unable to agree, by a certified public accountant appointed by the Presiding Judge of the San Mateo County Superior Court upon the application of either Landlord or Tenant (with notice to the other party). In either event, such certified public accountant shall be one who is not then employed in any capacity by Landlord or Tenant or by any of their respective affiliates. The audit shall be limited to the determination of the amount of Operating Expenses for the subject Lease Year, and shall be based on generally accepted accounting principles and tax accounting principles, consistently applied. If it is determined, by mutual agreement of Landlord and Tenant or by independent audit, that the amount of Operating Expenses billed to or paid by Tenant for the applicable Lease Year was incorrect, then the appropriate party shall pay to the other party the deficiency or overpayment, as applicable, within thirty (30) days after the final determination of such deficiency or overpayment. All costs and expenses of the audit shall be paid by Tenant unless the audit shows that Landlord overstated Operating Expenses for the subject Lease Year by more than five percent (5 %), in which case Landlord shall pay all costs and expenses of the audit. Each party agrees to maintain the confidentiality of the findings of any audit in accordance with the provisions of this Section 7.4.

7.5 PRORATION. If the Rent Commencement Date falls on a day other than the first day of a Lease Year or if this Lease terminates on a day other than the last day of a Lease Year, then the amount of Operating Expenses payable by Tenant with respect to such first or last partial Lease Year shall be prorated on the basis which the number of days during such Lease Year in which this Lease is in effect bears to 365. The termination of this Lease shall not affect the obligations of Landlord and Tenant pursuant to Section 7.4 to be performed after such termination.

8. UTILITIES

8.1 PAYMENT. Commencing with the Rent Commencement Date and thereafter throughout the term of this Lease, Tenant shall pay, before delinquency, all charges for water, gas, heat, light, electricity, power, sewer, telephone, alarm system, janitorial and

other services or utilities supplied to or consumed in or with respect to the Building (other than any separately metered costs for water, electricity or other services or utilities furnished with respect to the Common Areas, which costs shall be paid by Landlord and shall constitute Operating Expenses under Section 7.2 hereof), including any taxes on such services and utilities. It is the intention of the parties that all such services shall be separately metered to the Building. In the event that any of such services supplied to the Building are not separately metered, then the amount thereof shall be an item of Operating Expenses and shall be paid as provided in Article 7.

8.2 INTERRUPTION. There shall be no abatement of rent or other charges required to be paid hereunder and Landlord shall not be liable in damages or otherwise for interruption or failure of any service or utility furnished to or used with respect to the Building or Property because of accident, making of repairs, alterations or improvements, severe weather, difficulty or inability in obtaining services or supplies, labor difficulties or any other cause. Notwithstanding the foregoing provisions of this Section 8.2, however, in the event of any interruption or failure of any service or utility to the Building that (i) is caused in whole or in material part by the active negligence or willful misconduct of Landlord or its agents or employees AND (ii) continues for more than three (3) business days AND (iii) materially impairs Tenant's ability to use the Building for its intended purposes hereunder, then following such three (3) business day period, Tenant's obligations for payment of rent and other charges under this Lease shall be abated in proportion to the degree of impairment of Tenant's use of the Building, and such abatement shall continue until Tenant's use of the Building is no longer materially impaired thereby.

9. ALTERATIONS; SIGNS

9.1 RIGHT TO MAKE ALTERATIONS. Tenant shall make no alterations, additions or improvements to the Building or the Property, other than interior non-structural alterations costing less than Fifty Thousand Dollars ($50,000.00) in the aggregate during any twelve (12) month period, without the prior written consent of Landlord, which consent shall not be unreasonably withheld or delayed. All such alterations, additions and improvements shall be completed with due diligence in a first-class workmanlike manner, in compliance with plans and specifications approved in writing by Landlord and in compliance with all applicable laws, ordinances, rules and regulations, and to the extent Landlord's consent is not otherwise required hereunder for such alterations, additions or improvements, Tenant shall give prompt written notice thereof to Landlord. Tenant shall cause any contractors engaged by Tenant for work in the Building or on the Property to maintain public liability and property damage insurance, and other customary insurance, with such terms and in such amounts as Landlord may reasonably

require, naming as additional insureds Landlord and any of its partners, shareholders, property managers and lenders designated by Landlord for this purpose, and shall furnish Landlord with certificates of insurance or other evidence that such coverage is in effect. Notwithstanding any other provisions of this Section 9. I, under no circumstances shall Tenant make any structural alterations or improvements, or any substantial changes to the roof or substantial equipment installations on the roof, or any substantial changes or alterations to the building systems, without Landlord's prior written consent (which consent shall not be unreasonably withheld or delayed). If Tenant so requests in seeking Landlord's consent to any alterations, additions or improvements, Landlord shall specify in granting such consent whether Landlord intends to require that Tenant remove such alterations, additions or improvements (or any specified portions thereof) upon expiration or termination of this Lease. Landlord shall receive no fee for supervision, profit, overhead or general conditions in connection with any alterations, additions or improvements constructed or installed by Tenant under this Lease, whether as part of the initial Tenant's Work under EXHIBIT C or otherwise.

9.2 TITLE TO ALTERATIONS. All alterations, additions and improvements installed in, on or about the Building or the Property shall become part of the Property and shall become the property of Landlord, unless Landlord elects to require Tenant to remove the same upon the termination of this Lease; PROVIDED, however, that the foregoing shall not apply to Tenant's movable furniture and equipment and trade fixtures. Tenant shall promptly repair

any damage caused by its removal of any such furniture, equipment or trade fixtures. Notwithstanding any other provisions of this Article 9, however, (a) under no circumstances shall Tenant have any right to remove from the Building or the Property, at the expiration or termination of this Lease, any lab benches, fume hoods, cold rooms or other similar improvements and equipment installed in the Building and paid for in whole or in part by Landlord, even if such equipment and improvements were installed by Tenant as part of Tenant's Work under EXHIBIT C and paid for by Tenant in the form of rent (but Tenant SHALL have the right to remove any such equipment and improvements installed entirely by Tenant at its own expense and paid for in cash by Tenant, without any contribution or reimbursement from Landlord and without any related rental obligation on the part of Tenant); and (b) if Tenant requests Landlord's written consent to any alterations, additions or improvements under Section 9.1 hereof and, in requesting such consent, asks that Landlord specify whether Landlord will require removal of such alterations, additions or improvements upon termination or expiration of this Lease, then Landlord shall not be entitled to require such removal unless Landlord specified its intention to do so at the time of granting of Landlord's consent to the requested alterations, additions or improvements.

9.3 TENANT FIXTURES. Subject to the final sentence of Section 9.2 and to Section 9.5, Tenant may install, remove and reinstall trade fixtures without Landlord's prior written consent, except that installation and removal of any fixtures which are affixed to the Building or the Property or which affect the exterior or structural portions of the Building or the building systems shall require Landlord's written approval, which approval shall not be unreasonably withheld or delayed. Subject to the provisions of Section 9.5, the foregoing shall apply to Tenant's signs, logos and insignia, all of which Tenant shall have the right to place and remove and replace (a) only with Landlord's prior written consent as to location, size and composition, which consent shall not be unreasonably withheld or delayed, and (b) only in compliance with all restrictions and requirements of applicable law and of any covenants, conditions and restrictions or other written agreements now or hereafter applicable to the Property. Tenant shall immediately repair any damage caused by installation and removal of fixtures under this Section 9.3.

9.4 NO LIENS. Tenant shall at all times keep the Building and the Property free from all liens and claims of any contractors, subcontractors, materialmen, suppliers or any other parties employed either directly or indirectly by Tenant in construction work on the Building or the Property. Tenant may contest any claim of lien, but only if, prior to such contest, Tenant either (i) posts security in the amount of the claim, plus estimated costs and interest, or (ii) records a bond of a responsible corporate surety in such amount as may be required to release the lien from the Building and the Property. Tenant shall indemnify, defend and hold Landlord harmless against any and all liability, loss, damage, cost and other expenses, including, without limitation, reasonable attorneys' fees, arising out of claims of any lien for work performed or materials or supplies furnished at the request of Tenant or persons claiming under Tenant.

9.5 SIGNS. Without limiting the generality of the provisions of Section 9.3 hereof, Tenant shall have the right to display its corporate name and logo on the Building and in front of the entrance to the Building, subject to Landlord's prior approval as to location, size, design and composition (which

approval shall not be unreasonably withheld or delayed), subject to the established sign criteria for the Center and subject to all restrictions and requirements of applicable law and of any covenants, conditions and restrictions or other written agreements now or hereafter applicable to the Property. Landlord is hereby deemed to have approved, as to location, any signage the location of which is expressly designated on the Site Plan attached hereto as EXHIBIT B or on any Approved Plan developed pursuant to the Workletter.

10. MAINTENANCE AND REPAIRS

10.1 LANDLORD'S WORK.

(a) Landlord shall repair and maintain or cause to be repaired and maintained the Common Areas of the Center and the roof (structural portions only), exterior walls and other structural portions of the Building. The cost of all work performed by Landlord under this Section I0.1 shall be an Operating Expense hereunder, except to the extent such work (i) is required due to the negligence of Landlord, (ii) involves the repair or correction of a condition or defect that Landlord is required to correct pursuant to Section 5.2 hereof, (iii) is a capital expense not includible as an Operating Expense under Section 7.2 hereof, (iv) is required due to the negligence or willful misconduct of Tenant or its agents, employees or invitees (in which event Tenant shall bear the full cost of such work pursuant to the indemnification provided in Section 12.6 hereof, subject to the release set forth in Section 12.4 hereof). Tenant knowingly and voluntarily waives the right to make repairs at Landlord's expense, except to the extent permitted by Section 10.1 (b) below, or to offset the cost thereof against rent, under any law, statute, regulation or ordinance now or hereafter in effect.

(b) If Landlord fails to perform any repairs or maintenance required to be performed by Landlord on the Building under Section 10. l(a) and such failure continues for thirty (30) days or more after Tenant gives Landlord written notice of such failure (or, if such repairs or maintenance cannot reasonably be performed within such 30-day period, then if Landlord fails to commence performance within such 30-day period and thereafter to pursue such performance diligently to completion), then Tenant shall have the right to perform such repairs or maintenance and Landlord shall reimburse Tenant for the reasonable cost thereof within fifteen (15) days after written notice from Tenant of the completion and cost of such work, accompanied by copies of invoices or other reasonable supporting documentation. Under no circumstances, however, shall Tenant have any right to offset the cost of any such work against rent or other charges falling due from time to time under this Lease.

10.2 TENANT'S OBLIGATION FOR MAINTENANCE.

(a) GOOD ORDER, CONDITION AND REPAIR. Except as provided in Section 10.1 hereof, Tenant at its sole cost and expense shall keep and maintain in good and sanitary order, condition and repair the Building and every part thereof, wherever located, including but not limited to the roof (non-structural portions only), signs, interior, ceiling, electrical system, plumbing system, telephone and communications systems of the Building, the HVAC equipment and related mechanical systems serving the Building (for which equipment and systems Tenant shall enter into a service contract with a person or entity designated or approved by Landlord), all doors, door checks, windows, plate glass, door fronts, exposed plumbing and sewage and other utility facilities, fixtures, lighting, wall surfaces, floor surfaces and ceiling surfaces of the Building and all other interior repairs, foreseen and unforeseen, with respect to the Building, as required.

(b) LANDLORD'S REMEDY. If Tenant, after notice from Landlord, fails to make or perform promptly any repairs or maintenance which are the obligation of Tenant hereunder, Landlord shall have the right, but shall not be required, to enter the Building and make the repairs or perform the maintenance necessary to restore the Building to good and sanitary order, condition and repair. Immediately on demand from Landlord, the cost of such repairs shall be due and payable by Tenant to Landlord.

(c) CONDITION UPON SURRENDER. At the expiration or sooner termination of this Lease, Tenant shall surrender the Building and the Improvements, including any additions, alterations and improvements thereto, broom clean, in good and sanitary order, condition and repair, ordinary wear and tear excepted, first, however, removing all goods and effects of Tenant and all and fixtures and items required to be removed or specified to be removed at Landlord's election pursuant to this Lease (including, but not limited to, any such,, removal required as a result of an election duly made by Landlord to require such removal as

contemplated in Section 9.2), and repairing any damage caused by such removal. Tenant shall not have the right to remove fixtures or equipment if Tenant is in default hereunder unless Landlord specifically waives this provision in writing. Tenant expressly waives any and all interest in any personal property and trade fixtures not removed from the Property by Tenant at the expiration or termination of this Lease, agrees that any such personal property and trade fixtures may, at Landlord's election, be deemed to have been abandoned by Tenant, and authorizes Landlord (at its election and without prejudice to any other remedies under this Lease or under applicable law) to remove and either retain, store or dispose of such property at Tenant's cost and expense, and Tenant waives all claims against Landlord for any damages resulting from any such removal, storage, retention or disposal.

11. USE OF PROPERTY

11.1 PERMITTED USE. Subject to Sections 11.3, 11.4 and 11.6 hereof, Tenant shall use the Building solely for a laboratory research and development facility, including (but not limited to) wet chemistry and biology labs, clean rooms, pilot scale, clinical scale and GMP scale manufacturing, storage and use of toxic and radioactive materials (subject to the provisions of Section 11.6 hereof), storage and use of laboratory animals, administrative offices, and other lawful purposes reasonably related to or incidental to such specified uses (subject in each case to receipt of all necessary approvals from the City of South San Francisco and other governmental agencies having jurisdiction over the Building), and for no other purpose.

11.2 [Omitted.]

11.3 NO NUISANCE. Tenant shall not use the Property for or carry on or permit upon the Property or any part thereof any offensive, noisy or dangerous trade, business, manufacture, occupation, odor or fumes, or any nuisance or anything against public policy, nor interfere with the rights or business of Landlord in the Building or the Property, nor commit or allow to be committed any waste in, on or about the Property. Tenant shall not do or permit anything to be done in or about the Property, nor bring nor keep anything therein, which will in any way cause the Property to be uninsurable with respect to the insurance required by this Lease or with respect to standard fire and extended coverage insurance with vandalism, malicious mischief and riot endorsements.

11.4 COMPLIANCE WITH LAWS. Tenant shall not use the Property or permit the Property or the Center to be used in whole or in part for any purpose or use that is in violation of any applicable laws, ordinances, regulations or rules of any governmental agency or public authority. Tenant shall keep the Building and Improvements equipped with all safety appliances required by law, ordinance or insurance on the Property, or any order or regulation of any public authority, because of Tenant's particular use of the Property. Tenant shall procure all licenses and permits required for use of the Property. Tenant shall use the Property in strict accordance with all applicable ordinances, rules, laws and regulations and shall comply with all requirements of all governmental authorities now in force or which may hereafter be in force pertaining to the use of the Property by Tenant, including, without limitation, regulations applicable to noise, water, soil and air pollution, and making such nonstructural alterations and additions thereto as may be required from time to time by such laws, ordinances, rules, regulations and requirements of governmental authorities or insurers of the Property (collectively, "REQUIREMENTS") because of Tenant's construction of improvements in or other particular use of the Property. Any structural alterations or additions required from time to time by applicable Requirements because of Tenant's construction of improvements in the Building or other particular use of the Property shall, at Landlord's election, either (i) be made by Tenant, at Tenant's sole cost and expense, in accordance with the procedures and standards set forth in Section 9.1 for alterations by Tenant, or (ii) be made by Landlord at Tenant's sole cost and expense, in which event Tenant shall pay to Landlord as additional rent, within ten (10) days after demand by Landlord, an amount equal to all reasonable costs incurred by Landlord in connection with such alterations or additions, The judgment of any court, or the admission by Tenant in any proceeding against Tenant, that Tenant has violated any law, statute, ordinance or

governmental rule, regulation or requirement shall be conclusive of such violation as between Landlord and Tenant.

11.5 LIQUIDATION SALES. Tenant shall not conduct or permit to be conducted any auction, bankruptcy sale, liquidation sale, or going out of business sale, in, upon or about the Property, whether said auction or sale be voluntary, involuntary or pursuant to any assignment for the benefit of creditors, or pursuant to any bankruptcy or other insolvency proceeding.

11.6 ENVIRONMENTAL MATTERS.

(a) For purposes of this Section, "HAZARDOUS SUBSTANCE" shall mean the substances included within the definitions of the term "hazardous substance" under (i) the Comprehensive Environmental Response, Compensation and Liability Act of 1980, as amended, 42 U.S.C. Sections 9601 ET SEQ., and the regulations promulgated thereunder, as amended, (ii) the California Carpenter-Presley-Tanner Hazardous Substance Account Act, California Health & Safety Code Sections 25300 ET SEQ., and regulations promulgated thereunder, as amended, (iii) the Hazardous Materials Release Response Plans and Inventory Act, California Heath & Safety Code Sections 25500 ET SEQ., and regulations promulgated thereunder, as amended, and (iv) petroleum; "HAZARDOUS WASTE" shall mean (i) any waste listed as or meeting the identified characteristics of a "hazardous waste" under the Resource Conservation and Recovery Act of 1976, 42 U.S.C. Sections 6901 ET SEQ., and regulations promulgated pursuant thereto, as amended (collectively, "RCRA"), (ii) any waste meeting the identified characteristics of "hazardous waste," "extremely hazardous waste" or "restricted hazardous waste" under the California Hazardous Waste Control Law, California Health & Safety Code Sections 25100 ET SEQ., and regulations promulgated pursuant thereto, as amended (collectively, the "CHWCL"), and/or (iii) any waste meeting the identified characteristics of "medical waste" under California Health & Safety Code Sections 25015-25027.8, and regulations promulgated thereunder, as amended; and "HAZARDOUS WASTE FACILITY" shall mean a hazardous waste facility as defined under the CHWCL.

(b) Without limiting the generality of the obligations set forth in Section 11.4 of this Lease:

(i) Tenant shall not cause or permit any hazardous substance or hazardous waste to be brought upon, kept, stored or used in or about the Property without the prior written consent of Landlord, which consent shall not be unreasonably withheld, except that Tenant, in connection with its permitted use of the Property as provided in Section 11.1, may keep, store and use materials that constitute hazardous substances which are customary for such permitted use, provided such hazardous substances are kept, stored and used in quantities which are customary for such permitted use and are kept, stored and used in full compliance with clauses (ii) and (iii) immediately below.

(ii) Tenant shall comply with all applicable laws, rules, regulations, orders, permits, licenses and operating plans of any governmental authority with respect to the receipt, use, handling, generation, transportation, storage, treatment and/or disposal of hazardous substances or wastes by Tenant or its agents or employees, and Tenant will provide Landlord with copies of all permits, licenses, registrations and other similar documents that authorize Tenant to conduct any such activities in connection with its authorized use of the Property from time to time.

(iii) Tenant shall not (A) operate on or about the Property any facility required to be permitted or licensed as a hazardous waste facility or for which interim status as such is required, nor (B) store any hazardous wastes on or about the Property for ninety (90) days or more, nor (C) conduct any other activities on or about the Property that could result in the Property being deemed to be a "hazardous waste facility"(including, but not limited to, any storage or treatment of hazardous substances or hazardous wastes which could have such a result).

(iv) Tenant shall comply with all applicable laws, rules, regulations, orders and permits relating to underground storage tanks installed by Tenant or its agents or employees or at the request of Tenant (including any installation, monitoring, maintenance, closure and/or removal of such tanks) as such tanks are defined in California Health & Safety Code Section 25281(x), including, without limitation, complying with California Health & Safety Code Sections 25280-25299.7 and the regulations promulgated thereunder, as amended. Tenant shall furnish to Landlord copies of all registrations and permits issued to or held by Tenant from time to time for any and all underground storage tanks located on or under the Property.

(v) If applicable, Tenant shall provide Landlord in writing the following information and/or documentation within fifteen (15) days after the Rent Commencement Date, and shall update such information at least annually, on or before each anniversary of the Rent Commencement Date, to reflect any change in or addition to the required information and/or documentation (PROVIDED, however, that in the case of the materials described in subparagraphs (B), (C) and (E) below, Tenant shall not be required to deliver copies of such materials to Landlord but shall maintain copies of such materials to such extent and for such periods as may be required by applicable law and shall permit Landlord or its representatives to inspect and copy such materials during normal business hours at any time and from time to time upon reasonable notice to Tenant):

(A) A list of all hazardous substances and/or wastes that Tenant receives, uses, handles, generates, transports, stores, treats or

disposes of from time to time in connection with its operations on the Property.

(B) All Material Safety Data Sheets ("MSDS'S"), if any, required to be completed with respect to operations of Tenant at the Property from time to time in accordance with Title 26, California Code of Regulations Section 8-5194 or 42 U.S.C. Section 11021, or any amendments thereto, and any Hazardous Materials Inventory Sheets that detail the MSDS's.

(C) All hazardous waste manifests (as defined in Title 26, California Code of Regulations Section 22-66481), if any, that Tenant is required to complete from time to time in connection with its operations at the Property.

(D) A copy of any Hazardous Materials Management Plan required from time to time with respect to Tenant's operations at the Property, pursuant to California Health & Safety Code Sections 25500 ET SEQ., and any regulations promulgated thereunder, as amended.

(E) Any Contingency Plans and Emergency Procedures required of Tenant from time to time due to its operations in accordance with Title 26, California Code of Regulations Sections 22-67140 ET SEQ., and any amendments thereto, and any Training Programs and Records required under Title 26, California Code of Regulations, Section 22-67105, and any amendments thereto.

(F) Copies of any biennial reports to be furnished to the California Department of Health Services from time to time relating to hazardous substances or wastes, pursuant to Title 26, California Code of Regulations, Section 22-66493, and any amendments thereto.

(G) Copies of all industrial wastewater discharge permits issued to or held by Tenant from time to time in connection with its operations on the Property.

(H) Copies of any other lists or inventories of hazardous substances and/or wastes on or about the Property that Tenant is otherwise required to prepare and file from time to time with any governmental or regulatory authority.

(vi) Tenant shall secure Landlord's prior written approval for any proposed receipt, storage, possession, use, transfer or disposal of "radioactive materials" or "radiation," as such materials are defined in Title 26, California Code of Regulations Section 17-30100, and/or any other materials possessing the characteristics of the materials so defined, which approval Landlord may withhold in its sole and absolute discretion; PROVIDED, that such approval shall not be required for any radioactive materials for which Tenant has secured prior written approval of the Nuclear Regulatory Commission and delivered to Landlord a copy of such approval. Tenant, in connection with any such authorized receipt, storage, possession, use, transfer or disposal of radioactive materials or radiation, shall:

(A) Comply with all federal, state and local laws, rules, regulations, orders, licenses and permits issued to or applicable to Tenant with respect to its business operations on the Property;

(B) Maintain, to such extent and for such periods as may be required by applicable law, and permit Landlord and its representatives to inspect during normal business hours at any time and from time to time upon reasonable notice to Tenant, a list of all radioactive materials or radiation received, stored, possessed, used, transferred or disposed of by Tenant or in connection with the operation of Tenant's business on the Property from time to time, to the extent not already disclosed through delivery of a copy of a Nuclear Regulatory Commission approval with respect thereto as contemplated above; and

(C) Maintain, to such extent and for such periods as may be required by applicable law, and permit Landlord or its representatives to inspect during normal business hours at any time and from time to time upon reasonable notice to Tenant, all licenses, registration materials, inspection reports, governmental orders and permits in connection with the receipt, storage, possession, use, transfer or disposal of radioactive materials or radiation by Tenant or in connection with the operation of Tenant's business on the Property from time to time.

(vii) Tenant shall comply with any and all applicable laws, rules, regulations and orders of any governmental authority with respect to the release into the environment of any hazardous wastes or substances or radiation or radioactive materials by Tenant or its agents or employees. Tenant shall give Landlord immediate verbal notice of any unauthorized release of any such hazardous wastes or substances or radiation or radioactive materials into the environment, and shall follow such verbal notice with written notice to Landlord of such release within twenty-four

(24) hours of the time at which Tenant became aware of such release.

(viii) Tenant shall indemnify, defend and hold Landlord harmless from and against any and all claims, losses (including, but not limited to, loss of rental income), damages, liabilities, costs, legal fees and expenses of any sort arising out of or relating to (A) any failure by Tenant to comply with any provisions of this paragraph l l.6(b), or (B) any receipt, use handling, generation, transportation, storage, treatment, release and/or disposal of any hazardous substance or waste or any radioactive material or radiation on or about the Property as a proximate result of Tenant's use of the Property or as a result of any intentional or negligent acts or omissions of Tenant or of any agent, employee or invitee of Tenant.

(ix) Tenant shall cooperate with Landlord in furnishing Landlord with complete information regarding Tenant's receipt, handling, use, storage, transportation, generation, treatment and/or disposal of any hazardous substances or wastes or radiation or radioactive materials. Upon request, Tenant shall grant Landlord reasonable access at reasonable times to the Property to inspect Tenant's receipt, handling, use, storage, transportation, generation, treatment and/or disposal of hazardous substances or wastes or radiation or radioactive materials, without being deemed guilty of any disturbance of Tenant's use or possession and without being liable to Tenant in any manner.

(x) Notwithstanding Landlord's rights of inspection and review under this paragraph 11.6(b), Landlord shall have no obligation or duty to so inspect or

review, and no third party shall be entitled to rely on Landlord to conduct any sort of inspection or review by reason of the provisions of this paragraph 11.6(b).

(xi) If Tenant receives, handles, uses, stores, transports, generates, treats and/or disposes of any hazardous substances or wastes or radiation or radioactive materials on or about the Property at any time during the term of this Lease, then within thirty (30) days after the termination or expiration of this Lease, Tenant at its sole cost and expense shall obtain and deliver to Landlord an environmental study, performed by an expert reasonably satisfactory to Landlord, evaluating the presence or absence of hazardous substances and wastes, radiation and radioactive materials on and about the Property. Such study shall be based on a reasonable and prudent level of tests and investigations of the Property and surrounding portions of the Center (if appropriate), which tests shall be conducted no earlier than the date of termination or expiration of this Lease. Liability for any remedial actions required or recommended on the basis of such study shall be allocated in accordance with Sections 11.4, 11.6, 12.6 and other applicable provisions of this Lease.

(c) Landlord shall indemnify, defend and hold Tenant harmless from and against any and all claims, losses, damages, liabilities, costs, legal fees and expenses of any sort arising out of or relating to (i) the presence on the Property of any hazardous substances or wastes or radiation or radioactive materials as of the Rent Commencement Date (other than as a result of any intentional or negligent acts or omissions of Tenant or of any agent, employee or invitee of Tenant), (ii) any unauthorized release into the environment (including, but not limited to, the Property) of any hazardous substances or wastes or radiation or radioactive materials to the extent such release results from the negligence of or willful misconduct or omission by Landlord or its agents or employees, and/or (iii) the presence on the Property of any hazardous substances or wastes or radiation or radioactive materials arising after the Rent Commencement Date from any cause or source other than as a result of any intentional or negligent acts or omissions of Tenant or of any agent, employee or invitee of Tenant.

(d) The provisions of this Section 11.6 shall survive the termination of this Lease.

12. INSURANCE AND INDEMNITY

12.1 INSURANCE.

(a) Tenant shall procure and maintain in full force and effect at all times during the term of this Lease, at Tenant's cost and expense, commercial general liability insurance to protect against liability to the public, or to any invitee of Tenant or Landlord, arising out of or related to the use of or resulting from any accident occurring in, upon or about the Property, with limits of liability of not less than (i) Two Million Dollars ($2,000,000.00) for injury to or death of one person, (ii) Five Million Dollars ($5,000,000.00) for personal injury or death, per occurrence, and (iii) One Million Dollars ($1,000,000.00) for property damage, or combined single limit of liability of not less than Five Million Dollars

($5,000,000.00). Such insurance shall name Landlord, its general partners, its Managing Agent and any lender holding a deed of trust on the Property from time to time (as designated in writing by Landlord to Tenant from time to time) as additional insureds thereunder. The amount of such insurance shall not be construed to limit any liability or obligation of Tenant under this Lease. Tenant shall also procure and maintain in full force and effect at all times during the term of this Lease, at Tenant's cost and expense, products/completed operations coverage on terms and in amounts (A) customary in Tenant's industry for companies engaged in the marketing of products on a scale comparable to that in which Tenant is engaged from time to time and (B) mutually satisfactory to Landlord and Tenant in their respective reasonable discretion.

(b) Landlord shall procure and maintain in full force and effect at all times during the term of this Lease, at Landlord's cost and expense (but reimbursable as an Operating Expense under Section 7.2 hereof), commercial general liability insurance to

protect against liability arising out of or related to the use of or resulting from any accident occurring in, upon or about the Property, with combined single limit of liability of not less than Five Million Dollars ($5,000,000.00) per occurrence for bodily injury and property damage.

(c) Landlord shall procure and maintain in full force and effect at all times during the term of this Lease, at Landlord's cost and expense (but reimbursable as an Operating Expense under Section 7.2 hereof), policies of property insurance providing protection against "all risk of direct physical loss" (as defined by and detailed in the Insurance Service Office's Commercial Property Program "Cause of Loss--Special Form [CP1030]" or its equivalent) for the Building Shell (as defined in EXHIBIT C) and for the improvements in the Common Areas of the Property, on a full replacement cost basis (with no co-insurance or, if coverage without co-insurance is not reasonably available, then on an "agreed amount" basis). Such insurance may include earthquake coverage to the extent Landlord in its discretion elects to carry such coverage, and shall have such commercially reasonable deductibles and other terms as Landlord in its discretion determines to be appropriate. Landlord shall have no obligation to carry property damage insurance for any alterations, additions or improvements installed by Tenant in the Building or on or about the Property.

(d) Tenant shall procure and maintain in full force and effect at all times during the term of this Lease, at Tenant's cost and expense, policies of property insurance providing protection against "all risk of direct physical loss" (as defined by and detailed in the Insurance Service Office's Commercial Property Program "Cause of Loss-Special Form [CP1030]" or its equivalent) for the Tenant Improvements constructed by Tenant pursuant to EXHIBIT C and on all other alterations, additions and improvements installed by Tenant from time to time in or about the Building, on a full replacement cost basis (with no co-insurance or, if coverage without co-insurance is not reasonably available, then on an "agreed amount" basis). Such insurance may have such commercially reasonable deductibles and other terms as Tenant in its discretion determines to be appropriate, and shall name both Tenant and Landlord as insureds as their interests may appear.

(e) During the course of construction of the improvements being constructed by Landlord and Tenant under Section 5.1 and EXHIBIT C, Landlord and Tenant respectively shall each procure and maintain in full force and effect, at its respective sole cost and expense, policies of builder's risk insurance on the improvements respectively being constructed by it, in such amounts and with such commercially reasonable deductibles and other terms as Landlord in its reasonable discretion determines to be appropriate with respect to the insurance to be maintained by Landlord, and in such amounts and with such commercially reasonable deductibles and other terms as Landlord and Tenant may mutually and reasonably determine to be appropriate with respect to the insurance to be maintained by Tenant.

12.2 QUALITY OF POLICIES AND CERTIFICATES. All policies of insurance required hereunder shall be issued by responsible insurers and, in the case of policies carried or required to be carried by Tenant, shall be written as primary policies not contributing with and not in excess of any coverage that Landlord may carry. Tenant shall deliver to Landlord copies of policies or certificates of insurance showing that said policies are in effect. The coverage provided by such policies shall include the clause or endorsement referred to in Section 12.4. If Tenant fails to acquire, maintain or renew any insurance required to be maintained by it under this Article 12 or to pay the premium therefor, then Landlord, at its option and in addition to its other remedies, but without obligation so to do, may procure such insurance, and any sums expended by it to procure any such insurance on behalf of or in place of Tenant shall be repaid upon demand, with interest as provided in Section 3.2 hereof. Tenant shall obtain written undertakings from each insurer under policies required to be maintained by it to notify all insureds thereunder at least thirty (30) days prior to cancellation of coverage.

12.3 WORKERS' COMPENSATION. Tenant shall maintain in full force and effect during the term of this Lease workers' compensation insurance in at least the minimum amounts required by law, coveting all of Tenant's employees working on the Property.

12.4 WAIVER OF SUBROGATION. To the extent permitted by law and without affecting the coverage provided by insurance required to be maintained hereunder, Landlord and Tenant each waive any tight to recover against the other with respect to (i) damage to property, (ii) damage to the Property or any part thereof, or (iii) claims arising by reason of any of the foregoing, but only to the extent that any of the foregoing damages and claims under clauses (i)-(iii) hereof are covered, and only to the extent of such coverage, by casualty insurance actually carried or required to be carried hereunder by either Landlord or Tenant. This provision is intended to waive fully, and for the benefit of each party, any rights and claims which might give rise to a right of subrogation in any insurance carrier. Each party shall procure a clause or endorsement on any casualty insurance policy denying to the insurer rights of subrogation against the other party to the extent rights have been waived by the insured prior to the occurrence of injury or loss. Coverage provided by insurance maintained by Tenant shall not be limited, reduced or diminished by virtue of the subrogation waiver herein contained.

12.5 INCREASE IN PREMIUMS. Tenant shall do all acts and pay all expenses necessary to insure that the Property is not used for purposes prohibited by any applicable fire insurance, and that Tenant's use of the Property complies with all requirements necessary to obtain any such insurance. If Tenant uses or permits the Property to be used in a manner which increases the existing rate of any insurance carried by Landlord on the Center and such use continues for longer than a reasonable period specified in any written notice from Landlord to Tenant identifying the rate increase and the factors causing the same, then Tenant shall pay the amount of the increase in premium caused thereby, and Landlord's costs of obtaining other replacement insurance policies, including any increase in premium, within ten (10) days after demand therefor by Landlord.

12.6 INDEMNIFICATION.

(a) Tenant shall indemnify, defend and hold Landlord and its partners, shareholders, officers, directors, agents and employees harmless from any and all liability for injury to or death of any person, or loss of or damage to the property of any person, and all actions, claims, demands, costs (including, without limitation, reasonable attorneys' fees), damages or expenses of any kind arising therefrom which may be brought or made against Landlord or which Landlord may pay or incur by reason of the use, occupancy and enjoyment of the Property by Tenant or any invitees, sublessees, licensees, assignees, employees, agents or contractors of Tenant or holding under Tenant (including, but not limited to, any such matters arising out of or in connection with any early entry upon the Property by Tenant pursuant to Section 2.2 hereof) from any cause whatsoever other than negligence or willful misconduct or omission by Landlord, its agents or employees. Landlord and its partners, shareholders, officers, directors, agents and employees shall not be liable for, and Tenant hereby waives all claims against such persons for, damages to goods, wares and merchandise in or upon the Property, or for injuries to Tenant, its agents or third persons in or upon the Property, from any cause whatsoever other than negligence or willful misconduct or omission by Landlord, its agents or employees. Tenant shall give prompt notice to Landlord of any casualty or accident in, on or about the Property.

(b) Landlord shall indemnify, defend and hold Tenant and its partners, shareholders, officers, directors, agents and employees harmless from any and all liability for injury to or death of any person, or loss of or damage to the property of any person, and all actions, claims, demands, costs (including, without limitation, reasonable attorneys' fees), damages or expenses of any kind arising therefrom which may be brought or made against Tenant or which Tenant may pay or incur, to the extent such liabilities or other matters arise in, on or about the Property by reason of any negligence or willful misconduct or omission by Landlord, its agents or employees.

12.7 BLANKET POLICY. Any policy required to be maintained hereunder may be maintained under a so-called "blanket policy" insuring other parties and other locations so long as the amount of insurance required to be provided hereunder is not thereby diminished.

13. SUBLEASE AND ASSIGNMENT

13.1 ASSIGNMENT AND SUBLEASE OF BUILDING. Except in the case of a Permitted Transfer, Tenant shall not have the right or power to assign its interest in this Lease, or make any sublease of the Building or any portion thereof, nor shall any interest of Tenant under this Lease be assignable involuntarily or by

operation of law, without on each occasion obtaining the prior written consent of Landlord, which consent shall not be unreasonably withheld or delayed. Any purported sublease or assignment of Tenant's interest in this Lease requiring but not having received Landlord's consent thereto (to the extent such consent is required hereunder) shall be void. Without limiting the generality of the foregoing, Landlord may withhold consent to any proposed subletting or assignment solely on the ground, if applicable, that the use by the proposed subtenant or assignee is reasonably likely to. be incompatible with Landlord's use of any adjacent property owned or operated by Landlord, unless the proposed use is within the permitted uses specified in Section 11.1, in which event it shall not be reasonable for Landlord to object to the proposed use. Except in the case of a Permitted Transfer, any dissolution, consolidation, merger or other reorganization of Tenant, or any sale or transfer of substantially all of the stock or assets of Tenant in a single transaction or series of related transactions, shall be deemed to be an assignment hereunder and shall be void without the prior written consent of Landlord as required above. Notwithstanding the foregoing, (i) an initial public offering of the common stock of Tenant shall not be deemed to be an assignment hereunder; and (ii) Tenant shall have the right to assign this Lease or sublet the Building, or any portion thereof, without Landlord's consent (but with prior or concurrent written notice by Tenant to Landlord), to any Affiliate of Tenant, or to any entity which results from a merger or consolidation with Tenant, or to any entity which acquires substantially all of the stock or assets of Tenant as a going concern (hereinafter each a "PERMITTED TRANSFER"). For purposes of the preceding sentence, an "AFFILIATE" of Tenant shall mean any entity in which Tenant owns at least a twenty percent (20%) equity interest, any entity which owns at least a twenty percent (20%) equity interest in Tenant, and/or any entity which is related to Tenant by a chain of ownership interests involving at least a twenty percent (20%) equity interest at each level in the chain. Landlord shall have no right to terminate this Lease in connection with, and shall have no right to any sums or other economic consideration resulting from, any Permitted Transfer. Except as expressly set forth in this Section 13.1, however, the provisions of Section 13.2 shall remain applicable to any Permitted Transfer and the transferee under such Permitted Transfer shall be and remain subject to all of the terms and provisions of this Lease.

13.2 RIGHTS OF LANDLORD. Consent by Landlord to one or more assignments of this Lease, or to one or more sublettings of the Building or any portion thereof, or collection of rent by Landlord from any assignee or sublessee, shall not operate to exhaust Landlord's rights under this Article 13, nor constitute consent to any subsequent assignment or subletting. No assignment of Tenant's interest in this Lease and no sublease shall relieve Tenant of its obligations hereunder, notwithstanding any waiver or extension of time granted by Landlord to any assignee or sublessee, or the failure of Landlord to assert its rights against any assignee or sublessee, and regardless of whether Landlord's consent thereto is given or required to be given hereunder. In the event of a default by any assignee, sublessee or other successor of Tenant in the performance of any of the terms or obligations of Tenant under this Lease, Landlord may proceed directly against Tenant without the necessity of exhausting remedies against any such assignee, sublessee or other successor. In addition, Tenant immediately and irrevocably assigns to Landlord, as security for Tenant's obligations under this Lease, all rent from any subletting of all or a part of the Building as permitted under this Lease, and Landlord, as Tenant's assignee and as attorney-in-fact for Tenant, or any receiver for Tenant appointed on Landlord's application, may collect such rent and apply it toward Tenant's obligations under this Lease; except that, until the occurrence of an act of default by Tenant, Tenant shall have the right to collect such rent and to retain all sublease profits.

14. RIGHT OF ENTRY AND QUIET ENJOYMENT

14.1 RIGHT OF ENTRY. Landlord and its authorized representatives shall have the right to enter the Building at any time during the term of this Lease during normal business hours and upon not less than twenty-four (24) hours prior notice, except in the case of emergency (in which event no notice shall be required and entry may be made at any time), for the purpose of inspecting and determining the condition of the Building or for any other proper purpose including, without limitation, to make repairs, replacements or improvements which Landlord may deem necessary, to show the Building to prospective purchasers, to show the Building to prospective tenants (but only during the final year of the term of this Lease), and to post notices of nonresponsibility. Landlord shall not be liable for inconvenience, annoyance, disturbance, loss of business, quiet enjoyment or other damage or loss to Tenant by reason of making any repairs or performing any work upon the Building or the Property or by reason of erecting or maintaining any protective barricades in connection with any such work, and the obligations of Tenant under this Lease shall not thereby be affected in any manner whatsoever, PROVIDED, however, Landlord shall use reasonable efforts to minimize the inconvenience to Tenant's normal business operations caused thereby.

14.2 QUIET ENJOYMENT. Landlord covenants that Tenant, upon paying the rent and performing its obligations hereunder and subject to all the terms and conditions of this Lease, shall peacefully and quietly have, hold and enjoy the Building and the Property throughout the term of this Lease, or until this Lease is terminated as provided by this Lease.

15. CASUALTY AND TAKING

15.1 DAMAGE OR DESTRUCTION.

(a) If the Building, or the Common Areas of the Property necessary for Tenant's use and occupancy of the Building, are damaged or destroyed in whole or in part under circumstances in which (i) repair and restoration is permitted under applicable governmental laws, regulations and building codes then in effect and (ii) repair and restoration reasonably can be completed within a period of one (1) year (or, in the case of an occurrence during the last year of the term of this Lease, within a period of sixty (60) days) following the date of the occurrence, then Landlord, as to the Common Areas of the Property and the Building Shell, and Tenant, as to the Tenant Improvements constructed by Tenant, shall commence and complete, with all due diligence and as promptly as is reasonably practicable under the conditions then existing, all such repair and restoration as may be required to return the affected portions of the Property to a condition comparable to that existing immediately prior to the occurrence. In the event of damage or destruction the repair of which is not permitted under applicable governmental laws, regulations and building codes then in effect, if such damage or destruction (despite being corrected to the extent then permitted under applicable governmental laws, regulations and building codes) would still materially impair Tenant's ability to conduct its business in the Building, then either party may terminate this Lease as of the date of the occurrence by giving written notice to the other within thirty (30) days after the date of the occurrence; if neither party timely elects such termination, or if such damage or destruction does not materially impair Tenant's ability to conduct its business in the Building, then this Lease shall continue in full force and effect, except that there shall be an equitable adjustment in monthly minimum rental and of Tenant's Operating Cost Share of Operating Expenses, based upon the extent to which Tenant's ability to conduct its business in the Building is impaired, and Landlord and Tenant respectively shall restore the Common Areas and Building Shell and the Tenant Improvements to a complete architectural whole and to a functional condition. In the event of damage or destruction which cannot reasonably be repaired within one (1) year (or, in the case of an occurrence during the last year of the term of this Lease, within a period of sixty (60) days) following the date of the occurrence, then either Landlord or Tenant, at its election, may terminate this Lease as of the date of the occurrence by giving written notice to the other within thirty (30) days after the date of the occurrence; if neither party timely elects such termination, then this Lease shall continue in full force and effect and Landlord and Tenant

shall each repair and restore applicable portions of the Property in accordance with the first sentence of this Section 15.1.

(b) The respective obligations of Landlord and Tenant pursuant to Section 15.1(a) are subject to the following limitations:

(i) If the occurrence results from a peril which is required to be insured pursuant to Section 12.1(c) and (d) above, the obligations of either party shall not exceed the amount of insurance proceeds received from insurers (or, in the case of any failure to maintain required insurance, proceeds that reasonably would have been available if the required insurance had been maintained) by reason of such occurrence, plus the amount of the party's permitted deductible (PROVIDED that each party shall be obligated to use its best efforts to recover any available proceeds from the insurance which it is required to maintain pursuant to the provisions of Section 12.1(c) or (d), as applicable), and, if such proceeds (including, in the case of a failure to maintain required insurance, any proceeds that reasonably would have been available) are insufficient, either party may terminate file Lease unless the other party promptly elects and agrees, in writing, to contribute the amount of the shortfall; and

(ii) If the occurrence results from a peril which is not required to be insured pursuant to Section 12.1(c) and (d) above and is not actally insured, Landlord shall be required to repair and restore the Building Shell and Common Areas to the extent necessary for Tenant's continued use and occupancy of the Building, and Tenant shall be required to repair and restore the Tenant Improvements to the extent necessary for Tenant's continued use and occupancy of the Building, provided that each party's obligation to repair and restore shall not exceed an amount equal to five percent (5 %) of the replacement cost of the Building Shell and Common Area improvements, as to Landlord, or five percent (5 %) of the replacement cost of the Tenant Improvements, as to Tenant; if the replacement cost as to either party exceeds

such amount, then the party whose limit has been exceeded may terminate this Lease unless the other party promptly elects and agrees, in writing, to contribute the amount of the shortfall.

(c) If this Lease is terminated pursuant to the foregoing provisions of this Section 15.1 following an occurrence which is a peril actually insured or required to be insured against pursuant to Section 12.1(c) and (d), Landlord and Tenant agree (and any Lender shall be asked to agree) that such insurance proceeds shall be allocated between Landlord and Tenant in a manner which fairly and reasonably reflects their respective ownership rights under this Lease, as of the termination or expiration of the term of this Lease, with respect to the improvements, fixtures, equipment and other items to which such insurance proceeds are attributable.

(d) From and after the date of an occurrence resulting in damage to or destruction of the Building or of the Common Areas necessary for Tenant's use and occupancy of the Building, and continuing until repair and restoration thereof are completed, there shall be an equitable abatement of minimum rental and of Tenant's Operating Cost Share of Operating Expenses based upon the degree to which Tenant's ability to conduct its business in the Building is impaired.

15.2 CONDEMNATION.

(a) If during the term of this Lease the Property or Improvements, or any substantial part of either, is taken by eminent domain or by reason of any public improvement or condemnation proceeding, or in any manner by exercise of the right of eminent domain (including any transfer in avoidance of an exercise of the power of eminent domain), or receives irreparable damage by reason of anything lawfully done under color of public or other authority, then (i) this Lease shall terminate as to the entire Building at Landlord's election by written notice given to Tenant within sixty (60) days after the taking has occurred, and (ii) this Lease shall terminate as to the entire Building at Tenant's election, by written notice given to Landlord within thirty (30) days after the nature and extent of the taking have been finally determined, if the portion of the Building taken is of such extent and

nature as substantially to handicap, impede or permanently impair Tenant's use of the balance of the Building. If Tenant elects to terminate this Lease, Tenant shall also notify Landlord of the date of termination, which date shall not be earlier than thirty (30) days nor later than ninety (90) days after Tenant has notified Landlord of Tenant's election to terminate, except that this Lease shall terminate on the date of taking if such date falls on any date before the date of termination designated by Tenant. If neither party elects to terminate this Lease as hereinabove provided, this Lease shall continue in full force and effect (except that there shall be an equitable abatement of minimum rental and of Tenant's Operating Cost Share of Operating Expenses based upon the degree to which Tenant's ability to conduct its business in the Building is impaired), Landlord shall restore the Building Shell and Common Area improvements to a complete architectural whole and a functional condition and as nearly as reasonably possible to the condition existing before the taking, and Tenant shall restore the Tenant Improvements and Tenant's other alterations, additions and improvements to a complete architectural whole and a functional condition and as nearly as reasonably possible to the condition existing before the taking. In connection with any such restoration, each party shall use its respective best efforts (including, without limitation, any necessary negotiation or intercession with its respective lender, if any) to ensure that any severance damages or other condemnation awards intended to provide compensation for rebuilding or restoration costs are promptly collected and made available to Landlord and Tenant in portions reasonably corresponding to the cost and scope of their respective restoration obligations, subject only to such payment controls as either party or its lender may reasonably require in order to ensure the proper application of such proceeds toward the restoration of the Improvements. Each party waives the provisions of Code of Civil Procedure Section 1265.130, allowing either party to petition the Superior Court to terminate this Lease in the event of a partial condemnation of the Building or Property.

(b) The respective obligations of Landlord and Tenant pursuant to Section 15.2(a) are subject to the following limitations:

(i) Each party's obligation to repair and restore shall not exceed, net of any condemnation awards or other proceeds available for and allocable to such restoration as contemplated in Section 15.2(a), an amount equal to five percent (5 %) of the replacement cost of the Building Shell and Common Area improvements, as to Landlord, or five percent (5 %) of the replacement cost of the Tenant Improvements, as to Tenant; if the replacement cost as to either party exceeds such amount, then the party whose limit has been exceeded may terminate this Lease unless the other party promptly elects and agrees, in writing, to contribute the amount of the shortfall; and

(ii) If this Lease is terminated pursuant to the foregoing provisions of this Section 15.2, or if this Lease remains in effect but any condemnation awards or other proceeds become available as compensation for the loss or destruction of any of the Improvements, then Landlord and Tenant agree (and any Lender shall be asked to agree) that such proceeds shall be allocated between Landlord and Tenant, respectively, in the respective proportions in which Landlord and Tenant would have shared, under Section 15.1 (c), the proceeds of any insurance proceeds following loss or destruction of the applicable improvements by an insured casualty.

15.3 RESERVATION OF COMPENSATION. Landlord reserves, and Tenant waives and assigns to Landlord, all rights to any award or compensation for damage to the Improvements, the Property and the leasehold estate created hereby, accruing by reason of any taking in any public improvement, condemnation or eminent domain proceeding or in any other manner by exercise of the right of eminent domain or of anything lawfully done by public authority, except that (a) Tenant shall be entitled to any and all compensation or damages paid for or on account of Tenant's moving expenses, trade fixtures and equipment and any leasehold improvements installed by Tenant in the Building at its own sole expense, but only to the extent Tenant would have been entitled to remove such items at the expiration of the term of this Lease and then only to the extent of the then remaining unamortized value of such improvements computed on a straight-line basis over the term of this Lease, and (b) any condemnation awards or proceeds described in Section 15.2(b)(ii) shall be allocated

and disbursed in accordance with the provisions of Section 15.2(b)(ii), notwithstanding any contrary provisions of this Section 15.3.

15.4 RESTORATION OF IMPROVEMENTS. In connection with any repair or restoration of Improvements by either party following a casualty or taking as hereinabove set forth, the party responsible for such repair or restoration shall, to the extent possible, return such Improvements to a condition substantially equal to that which existed immediately prior to the casualty or taking. To the extent such party wishes to make material modifications to such Improvements, such modifications shall be subject to the prior written approval of the other party (not to be unreasonably withheld or delayed), except that no such approval shall be required for modifications that are required by applicable governmental authorities as a condition of the repair or restoration, unless such required modifications would impair or impede Tenant's conduct of its business in the Building (in which case any such modifications in Landlord's work shall require Tenant's consent, not unreasonably withheld or delayed) or would materially and adversely affect the exterior appearance, the structural integrity or the mechanical or other operating systems of the Building (in which case any such modifications in Tenant's work shall require Landlord's consent, not unreasonably withheld or delayed).

16. DEFAULT

16.1 EVENTS OF DEFAULT. The occurrence of any of the following shall constitute an event of default on the part of Tenant:

(a) [Omitted.]

(b) NONPAYMENT. Failure to pay, when due, any amount payable to Landlord hereunder, such failure continuing for a period of five (5) business days after written notice of such failure; PROVIDED, however, that any such notice shall be in lieu of, and not in addition to, any notice required under California Code of Civil Procedure Section 1161 ET SEQ., as amended from time to time;

(c) OTHER OBLIGATIONS. Failure to perform any obligation, agreement or covenant under this Lease other than those matters specified in subsection (b) hereof, such failure continuing for thirty (30) days after written notice of such failure; PROVIDED, however, that if such failure is curable in nature but cannot reasonably be cured within such 30-day period, then Tenant shall not be in default if, and so long as, Tenant promptly (and in all events within such 30-day period) commences such cure and thereafter diligently pursues such cure to completion; and PROVIDED FURTHER, however, that any such notice shall be in lieu of, and not in addition to, any notice required under California Code of Civil Procedure Section 1161 ET SEQ., as amended from time to time;

(d) GENERAL ASSIGNMENT. A general assignment by Tenant for the benefit of creditors;

(e) BANKRUPTCY. The filing of any voluntary petition in bankruptcy by Tenant, or the filing of an involuntary petition by Tenant's creditors, which involuntary petition remains undischarged for a period of thirty (30) days. In the event that under applicable law the trustee in bankruptcy or Tenant has the right to affirm this Lease and continue to perform the obligations of Tenant hereunder, such trustee or Tenant shall, in such time period as may be permitted

by the bankruptcy court having jurisdiction, cure all defaults of Tenant hereunder outstanding as of the date of the affirmance of this Lease and provide to Landlord such adequate assurances as may be necessary to ensure Landlord of the continued performance of Tenant's obligations under this Lease. Specifically, but without limiting the generality of the foregoing, such adequate assurances must include assurances that the Building continues to be operated only for the use permitted hereunder. The provisions hereof are to assure that the basic understandings between Landlord and Tenant with respect to Tenant's use of the Property and the benefits to Landlord therefrom are preserved, consistent with the purpose and intent of applicable bankruptcy laws;

(f) RECEIVERSHIP. The employment of a receiver appointed by court order to take possession of substantially all of Tenant's assets or the Building, if such receivership remains undissolved for a period of thirty (30) days;

(g) ATTACHMENT. The attachment, execution or other judicial seizure of all or substantially all of Tenant's assets or the Building, if such attachment or other seizure remains undismissed or undischarged for a period of thirty (30) days after the levy thereof; or

(h) INSOLVENCY. The admission by Tenant in writing of its inability to pay its debts as they become due, the filing by Tenant of a petition seeking any reorganization or arrangement, composition, readjustment, liquidation, dissolution or similar relief under any present or future statute, law or regulation, the filing by Tenant of an answer admitting or failing timely to contest a material allegation of a petition filed against Tenant in any such proceeding or, if within thirty (30) days after the commencement of any proceeding against Tenant seeking any reorganization or arrangement, composition, readjustment, liquidation, dissolution or similar relief under any present or future statute, law or regulation, such proceeding shall not have been dismissed.

16.2 REMEDIES UPON TENANT'S DEFAULT.

(a) Upon the occurrence of any event of default described in Section 16.1 hereof, Landlord, in addition to and without prejudice to any other rights or remedies it may have, shall have the immediate right to re-enter the Building or any part thereof and repossess the same, expelling and removing therefrom all persons and property (which property may be stored in a public warehouse or elsewhere at the cost and risk of and for the account of Tenant), using such force as may be necessary to do so (as to which Tenant hereby waives any claim for loss or damage that may thereby occur). In addition to or in lieu of such re-entry, and without prejudice to any other rights or remedies it may have, Landlord shall have the right either (i) to terminate this Lease and recover from Tenant all damages incurred by Landlord as a result of Tenant's default, as hereinafter provided, or (ii) to continue this Lease in effect and recover rent and other charges and amounts as they become due.

(b) Even if Tenant has breached this Lease and abandoned the Building, this Lease shall continue in effect for so long as Landlord does not terminate Tenant's right to possession under subsection (a) hereof and Landlord may enforce all of its rights and remedies under this Lease, including the right to recover rent as it becomes due, and Landlord, without terminating this Lease, may exercise all of the rights and remedies of a lessor under California Civil Code Section 1951.4 (lessor may continue lease in effect after lessee's breach and abandonment and recover rent as it becomes due, if lessee has right to sublet or assign, subject only to reasonable limitations), or any successor Code section. Acts of maintenance, preservation or efforts to relet the Building or the appointment of a receiver upon application of Landlord to protect Landlord's interests under this Lease shall not constitute a termination of Tenant's right to possession.

(c) If Landlord terminates this Lease pursuant to this Section 16.2, Landlord shall have all of the rights and remedies of a landlord provided by Section 1951.2 of the Civil Code of the State of California, or any successor Code section, which remedies include Landlord's right to recover from Tenant (i) the worth at the time of award of the unpaid rent and additional rent which had been earned at the time of termination, (ii) the worth at the time of award of the amount by which the unpaid rent and additional rent which would have been earned after termination until the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided, (iii) the worth at the time of award of the amount by which the unpaid rent and additional rent for the balance of the term after the time of award exceeds the amount of such rental loss that Tenant proves could be reasonably avoided, and (iv) any other amount necessary to compensate Landlord for all the detriment proximately caused by Tenant's failure to perform its obligations under this Lease or which in the ordinary course of-things would be likely to result therefrom, including, but not limited to, the cost of recovering possession of the Building, expenses of

reletting, including necessary repair, renovation and alteration of the Building, reasonable attorneys' fees, and other reasonable costs. The "WORTH AT THE TIME OF AWARD" of the amounts referred to in clauses (i) and (ii) above shall be computed by allowing interest at ten percent (10%) per annum from the date such amounts accrued to Landlord. The "WORTH AT THE TIME OF AWARD" of the amounts referred to in clause (iii) above shall be computed by discounting such amount at one percentage point above the discount rate of the Federal Reserve Bank of San Francisco at the time of award.

16.3 REMEDIES CUMULATIVE. All rights, privileges and elections or remedies of Landlord contained in this Article 16 are cumulative and not alternative to the extent permitted by law and except as otherwise provided herein.

17. SUBORDINATION, ATTORNMENT AND SALE

17.1 SUBORDINATION TO MORTGAGE. This Lease, and any sublease entered into by Tenant under the provisions of this Lease, shall be subject and subordinate to any ground lease, mortgage, deed of trust, sale/leaseback transaction or any other hypothecation for security now or hereafter placed upon the Building, the Property, the Center, or any of them, and the rights of any assignee of Landlord or of any ground lessor, mortgagee, trustee, beneficiary or leaseback lessor under any of the foregoing, and to any and all advances made on the security thereof and to all renewals, modifications, consolidations, replacements and extensions thereof; PROVIDED, however, that such subordination in the case of any future ground lease, mortgage, deed of trust, sale/leaseback transaction or any other hypothecation for security placed upon the Building, the Property, the Center, or any of them shall be conditioned on Tenant's receipt from the ground lessor, mortgagee, trustee, beneficiary or leaseback lessor of a Non-Disturbance Agreement in a form reasonably acceptable to Tenant (i) confirming that so long as Tenant is not in material default hereunder beyond any applicable cure period (for which purpose the occurrence of any event of default under Section 16.1 hereof shall be deemed to be "material"), Tenant's rights hereunder shall not be disturbed by such person or entity and (ii) agreeing that the benefit of such Non-Disturbance Agreement shall be transferable to any transferee under a Permitted Transfer and to any other assignee or subtenant that is acceptable to the ground lessor, mortgagee, trustee, beneficiary or leaseback lessor at the time of transfer. Moreover, Tenant's obligations under this Lease shall be conditioned on Tenant's receipt within thirty (30) days after mutual execution of this Lease, from (x) Slough Estates USA Inc. (as successor to Slough Parks Incorporated), the beneficiary under an existing deed of trust on the Property, and (y) any other ground lessor, mortgagee, trustee, beneficiary or leaseback lessor currently owning or holding a security interest in the Property, of a Non-Disturbance Agreement in a form reasonably acceptable to Tenant confirming (i) that so long as Tenant is not in material default hereunder beyond any applicable cure period (for which purpose the occurrence of any event of default under Section 16.1 hereof shall be deemed to be "material"), Tenant's rights hereunder shall not be disturbed by such person or entity and (ii) agreeing that the benefit of such Non-Disturbance Agreement shall be transferable to any transferee under a Permitted Transfer and to any other assignee or subtenant that is acceptable to the ground lessor, mortgagee, trustee, beneficiary or leaseback lessor at the time of transfer. If any mortgagee, trustee, beneficiary, ground lessor, sale/leaseback lessor or assignee elects to have this Lease be an encumbrance upon the Property prior to the lien of its mortgage, deed of trust, ground lease or leaseback lease or other security arrangement and gives notice thereof to Tenant, this Lease shall be deemed prior thereto, whether this Lease is dated prior or subsequent to the date thereof or the date of recording thereof. Tenant, and any sublessee, shall execute such documents as may reasonably be requested by any mortgagee, trustee, beneficiary, ground lessor, sale/leaseback lessor or assignee to evidence the subordination herein set forth, subject to the conditions set forth above, or to make this Lease prior to the lien of any mortgage, deed of trust, ground lease, leaseback lease or other security arrangement, as the case may be. Upon any default by Landlord in the performance of its obligations under any mortgage, deed of trust, ground lease, leaseback lease or assignment, Tenant (and any sublessee) shall, notwithstanding any subordination hereunder, attorn to the mortgagee, trustee, beneficiary, ground lessor, leaseback lessor or assignee thereunder upon demand and become the tenant of the successor in interest to Landlord, at

the option of such successor in interest, and shall execute and deliver any instrument or instruments confirming the attornment herein provided for.

17.2 SALE OF LANDLORD'S INTEREST. Upon sale, transfer or assignment of Landlord's entire interest in the Building and the Property, Landlord shall be relieved of its obligations hereunder with respect to liabilities accruing from and after the date of such sale, transfer or assignment.

17.3 ESTOPPEL CERTIFICATES. Tenant or Landlord (the "RESPONDING PARTY"), as applicable, shall at any time and from time to time, within ten (10) days after written request by the other party (the "REQUESTING PARTY"), execute, acknowledge and deliver to the requesting party a certificate in writing

stating: (i) that this Lease is unmodified and in full force and effect, or if there have been any modifications, that this Lease is in full force and effect as modified and stating the date and the nature of each modification; (ii) the date to which rental and all other sums payable hereunder have been paid; (iii) that the requesting party is not in default in the performance of any of its obligations under this Lease, that the certifying party has given no notice of default to the requesting party and that no event has occurred which, but for the expiration of the applicable time period, would constitute an event of default hereunder, or if the responding party alleges that any such default, notice or event has occurred, specifying the same in reasonable detail; and (iv) such other matters as may reasonably be requested by the requesting party or by any institutional lender, mortgagee, trustee, beneficiary, ground lessor, sale/leaseback lessor or prospective purchaser of the Property, or prospective sublessee or assignee of this Lease. Any such certificate provided under this Section 17.3 may be relied upon by any lender, mortgagee, trustee, beneficiary, assignee or successor in interest to the requesting party, by any prospective purchaser, by any purchaser on foreclosure or sale, by any grantee under a deed in lieu of foreclosure of any mortgage or deed of trust on the Property, by any subtenant or assignee, or by any other third party. Failure to execute and return within the required time any estoppel certificate requested hereunder, if such failure continues for five (5) days after a second written request by the requesting party for such estoppel certificate, shall be deemed to be an admission of the truth of the matters set forth in the form of certificate submitted to the responding party for execution.

17.4 SUBORDINATION TO CC&R'S. This Lease, and any permitted sublease entered into by Tenant under the provisions of this Lease, and the interests in real property conveyed hereby and thereby shall be subject and subordinate (a) to any declarations of covenants, conditions and restrictions affecting the Property or the Center from time to time, PROVIDED that the terms of such declarations are reasonable, do not materially impair Tenant's ability to conduct the uses permitted hereunder on the Property, and do not discriminate against Tenant relative to other similarly situated tenants occupying portions of the Center, (b) to the Declaration of Covenants, Conditions and Restrictions for Pointe Grand Business Park dated November 4, 1991 and recorded on February 25, 1992 as Instrument No. 92025214, Official Records of San Mateo County, as amended from time to time (the "MASTER DECLARATION"), the provisions of which Master Declaration are an integral part of this Lease, (c) to the Declaration of Covenants, Conditions and Restrictions dated November 23, 1987 and recorded on November 24, 1987 as Instrument No. 87177987, Official Records of San Mateo County, which declaration imposes certain covenants, conditions and restrictions on the Property, and (d) to the Environmental Restriction and Covenant (Pointe Grand) dated as of April 16, 1997 and recorded on April 16, 1997 as Instrument No. 97-043682, Official Records of San Mateo County, which declaration imposes certain covenants, conditions and restrictions on the Center. Tenant agrees to execute, upon request by Landlord, any documents reasonably required from time to time to evidence such subordination.

17.5 MORTGAGEE PROTECTION. If, following a default by Landlord under any mortgage, deed of trust, ground lease, leaseback lease or other security arrangement covering the Building, the Property, the Center, or any of them, the Building, the Property and/or the Center, as applicable, is acquired by the mortgagee, beneficiary, master lessor or other secured party, or by any other successor owner, pursuant to a foreclosure, trustee's sale, sheriffs sale, lease termination or other-similar procedure (or deed in lieu thereof), then any such person or entity so acquiring the Building, the Property and/or the Center shall not be:

(a) liable for any act or omission of a prior landlord or owner of the Property (including, but not limited to, Landlord);

(b) subject to any offsets or defenses that Tenant may have against any prior landlord or owner of the Property and/or the Center (including, but not limited to, Landlord);

(c) bound by any rent or additional rent that Tenant may have paid in advance to any prior landlord or owner of the Property and/or the Center (including, but not limited to, Landlord) for a period in excess of one month, or by any security deposit, cleaning deposit or other prepaid charge that Tenant may have paid in advance to any prior landlord or owner (including, but not limited to, Landlord), except to the extent such deposit or prepaid amount has been expressly turned over to or credited to the successor owner thus acquiring the Property and/or the Center, as applicable:

(d) liable for any warranties or representations of any nature whatsoever, whether pursuant to this Lease or otherwise, by any prior landlord or owner of the Property and/or the Center (including, but not limited to, Landlord) with respect to the use, construction, zoning, compliance with laws, title, habitability, fitness for purpose or possession, or physical condition (including, without limitation, environmental matters) of the Property, the Building or the Center; or

(e) liable to Tenant in any amount beyond the interest of such mortgagee, beneficiary, master lessor or other secured party or successor owner in the Property and the Center as they exist from time to time, it being the intent of this provision that Tenant shall look solely to the interest of any such mortgagee, beneficiary, master lessor or other secured party or successor owner in the Property and Center for the payment and discharge of the landlord's obligations under this Lease and that such mortgagee, beneficiary, master lessor or other secured party or successor owner shall have no separate personal liability for any such obligations.

18. SECURITY

18.1 DEPOSIT. Within ten (10) days after mutual execution of this Lease, Tenant shall deposit with Landlord the sum of One Hundred Twenty-One Thousand Nine Hundred Twenty-Eight and No/100 Dollars ($121,928.00), which sum (the "SECURITY DEPOSIT" shall be held by Landlord as security for the faithful performance of all of the terms, covenants, and conditions of this Lease to be kept and performed by Tenant during the term hereof. If Tenant defaults with respect to any provision of this Lease, including, without limitation, the provisions relating to the payment of rental and other sums due hereunder, Landlord shall have the right, but shall not be required, to use, apply or retain all or any part of the Security Deposit for the payment of rental or any other amount which Landlord may spend or become obligated to spend by reason of Tenant's default or to compensate Landlord for any other loss or damage which Landlord may suffer by reason of Tenant's default. If any portion of the Security Deposit is so used or applied, Tenant shall, within ten (10) days after written demand therefor, deposit cash with Landlord in an amount sufficient to restore the Security Deposit to its original amount and Tenant's failure to do so shall be a material breach of this Lease. Landlord shall not be required to keep any deposit under this Section separate from Landlord's general funds, and Tenant shall not be entitled to interest thereon. If Tenant fully and faithfully performs every provision of this Lease to be performed by it, the Security Deposit, or any balance thereof, shall be returned to Tenant or, at Landlord's option, to the last assignee of Tenant's interest hereunder, at the expiration of the term of this Lease and after Tenant has vacated the Property. In the event of termination of Landlord's interest in this Lease, Landlord shall transfer all deposits then held by Landlord under this Section to Landlord's successor in interest, whereupon Tenant agrees to release Landlord from all liability for the return of such deposit or the accounting thereof.

19. MISCELLANEOUS

19.1 NOTICES. All notices, consents, waivers and other communications which this Lease requires or permits either party to give to the other shall be in writing and shall be deemed given when delivered personally (including delivery by private courier or express delivery service) or four (4) days after deposit in the United States mail, registered or certified mail, postage prepaid, addressed to the parties at their respective addresses as follows:

To Tenant: (until Rent Commencement Date)
Rigel, Inc.
772 Lucerne Drive
Sunnyvale, CA 94086
Attn: James M. Gower

(after Rent Commencement Date)
Rigel, Inc.
[street address to be determined]
South San Francisco, CA 94080
Attn: James M. Gower

with copy to: Cooley Godward LLP
Five Palo Alto Square, 4th Floor
Palo Alto, CA 94306-2155
Attn: Anna B. Pope, Esq.

To Landlord: Britannia Pointe Grand Limited Partnership
1939 Harrison Street, Suite 715
Park Plaza Building
Oakland, CA 94612
Attn: T. J. Bristow

with copy to: Folger Levin & Kahn LLP
Embarcadero Center West
275 Battery Street, 23rd Floor
San Francisco, CA 94111
Attn: Donald E. Kelley, Jr.

and copy to: Slough Estates USA Inc.
33 West Monroe Street, Suite 2000
Chicago, IL 60603

Attn: William Rogalla

or to such other address as may be contained in a notice at least fifteen (15) days prior to the address change from either party to the other given pursuant to this Section. Rental payments and other sums required by this Lease to be paid by Tenant shall be delivered to Landlord at Landlord's address provided in this Section, or to such other address as Landlord may from time to time specify in writing to Tenant, and shall be deemed to be paid only upon actual receipt.

19.2 SUCCESSORS AND ASSIGNS. The obligations of this Lease shall run with the land, and this Lease shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns, except that the original Landlord named herein and each successive Landlord under this Lease shall be liable only for obligations accruing during the period of its ownership of the Property, and any liability for obligations accruing after termination Of such ownership shall terminate as of the date of such termination of ownership and shall pass to the successor lessor.

19.3 NO WAIVER. The failure of Landlord to seek redress for violation, or to insist upon the strict performance, of any covenant or condition of this Lease shall not be deemed at

waiver of such violation, or prevent a subsequent act which would originally have constituted a violation from having all the force and effect of an original violation.

19.4 SEVERABILITY. If any provision of this Lease or the application thereof is held to be invalid or unenforceable, the remainder of this Lease or the application of such provision to persons or circumstances other than those as to which it is invalid or unenforceable shall not be affected thereby, and each of the provisions of this Lease shall be valid and enforceable, unless enforcement of this Lease as so invalidated would be unreasonable or grossly inequitable under all the circumstances or would materially frustrate the purposes of this Lease.

19.5 LITIGATION BETWEEN PARTIES. In the event of any litigation or other dispute resolution proceedings between the parties hereto arising out of or in connection with this Lease, the prevailing party shall be reimbursed for all reasonable costs, including, but not limited to, reasonable accountants' fees and attorneys' fees, incurred in connection with such proceedings (including, but not limited to, any appellate proceedings relating thereto) or in connection with the enforcement of any judgment or award rendered in such proceedings. "PREVAILING PARTY" within the meaning of this Section shall include, without limitation, a party who dismisses an action for recovery hereunder in exchange for payment of the sums allegedly due, performance of covenants allegedly breached or consideration substantially equal to the relief sought in the action.

19.6 SURRENDER. A voluntary or other surrender of this Lease by Tenant, or a mutual termination thereof between Landlord and Tenant, shall not result in a merger but shall, at the option of Landlord, operate either as an assignment to Landlord of any and all existing subleases and subtenancies, or a termination of all or any existing subleases and subtenancies. This provision shall be contained in any and all assignments or subleases made pursuant to this Lease.

19.7 INTERPRETATION. The provisions of this Lease shall be construed as a whole, according to their common meaning, and not strictly for or against Landlord or Tenant. The captions preceding the text of each Section and subsection hereof are included only for convenience of reference and shall be disregarded in the construction or interpretation of this Lease.

19.8 ENTIRE AGREEMENT. This written Lease, together with the exhibits hereto, contains all the representations and the entire understanding between the parties hereto with respect to the subject matter hereof. Any prior correspondence, memoranda or agreements are replaced in total by this Lease and the exhibits hereto. This Lease may be modified only by an agreement in writing signed by each of the parties.

19.9 GOVERNING LAW. This Lease and all exhibits hereto shall be construed and interpreted in accordance with and be governed by all the provisions of the laws of the State of California.

19.10 NO PARTNERSHIP. The relationship between Landlord and Tenant is solely that of a lessor and lessee. Nothing contained in this Lease shall be construed as creating any type or manner of partnership, joint venture or joint enterprise with or between Landlord and Tenant.

19.11 FINANCIAL INFORMATION. From time to time Tenant shall promptly provide directly to prospective lenders and purchasers of the Property and/or Center designated by Landlord such financial information pertaining to the financial status of Tenant as Landlord may reasonably request; PROVIDED, Tenant

shall be permitted to provide such financial information in a manner which Tenant deems reasonably necessary to protect the confidentiality of such information. In addition, from time to time, Tenant shall provide Landlord with such financial information pertaining to the financial status of Tenant as Landlord may reasonably request. Landlord agrees that all financial information supplied to Landlord by Tenant shall be treated as confidential material, and shall not be disseminated to any party or entity (including any entity affiliated with Landlord) without Tenant's prior

written consent, except that Landlord shall be entitled to provide such information, subject to reasonable precautions to protect the confidential nature thereof, (i) to Landlord's partners and professional advisors, solely to use in connection with Landlord's execution and enforcement of this Lease, and (ii) to prospective lenders and/or purchasers of the Property and/or Center, solely for use in connection with their bona fide consideration of a proposed financing or purchase of the Property and/or Center, PROVIDED that such prospective lenders and/or purchasers are not then engaged in businesses directly competitive with the business then being conducted by Tenant. For purposes of this Section, without limiting the generality of the obligations provided herein, it shall be deemed reasonable for Landlord to request copies of Tenant's most recent audited annual financial statements, or, if audited statements have not been prepared, unaudited financial statements for Tenant's most recent fiscal year, accompanied by a certificate of Tenant's chief financial officer that such financial statements fairly present Tenant's financial condition as of the date(s) indicated. Notwithstanding any other provisions of this Section 19.11, during any period in which Tenant has outstanding a class of publicly traded securities and is filing with the Securities and Exchange Commission, on a regular basis, Forms 10Q and 10K and any other periodic filings required under the Securities Exchange Act of 1934, as amended, it shall constitute sufficient compliance under this Section 19.11 for Tenant to furnish Landlord with copies of such periodic filings substantially concurrently with the filing thereof with the Securities and Exchange Commission.

Landlord and Tenant recognize the need of Tenant to maintain the confidentiality of information regarding its financial status and the need of Landlord to be informed of, and to provide to prospective lenders and purchasers of the Property and/or Center financial information pertaining to, Tenant's financial status. Landlord and Tenant agree to cooperate with each other in achieving these needs within the context of the obligations set forth in this Section.

19.12 COSTS. If Tenant requests the consent of Landlord under any provision of this Lease for any act that Tenant proposes to do hereunder, including, without limitation, assignment or subletting of the Building, Tenant shall, as a condition to doing any such act and the receipt of such consent, reimburse Landlord promptly for any and all reasonable costs and expenses incurred by Landlord in connection therewith, including, without limitation, reasonable attorneys' fees, up to a maximum of $2,500.00 per request.

19.13 TIME. Time is of the essence of this Lease, and of every term and condition hereof.

19.14 RULES AND REGULATIONS. Tenant shall observe, comply with and obey, and shall cause its employees, agents and, to the best of Tenant's ability, invitees to observe, comply with and obey such rules and regulations as Landlord may promulgate from time to time for the safety, care, cleanliness, order and use of the Improvements, the Property and the Center.

19.15 BROKERS. Landlord agrees to pay a brokerage commission to Catalyst Real Estate Group and to Cornish & Carey Commercial in connection with the consummation of this Lease in accordance with a separate agreement. Each party represents and warrants that no other broker participated in the consummation of this Lease and agrees to indemnify, defend and hold the other party harmless against any liability, cost or expense, including, without limitation, reasonable attorneys' fees, arising out of any claims for brokerage commissions or other similar compensation in connection with any conversations, prior negotiations or other dealings by the indemnifying party with any other broker.

19.16 MEMORANDUM OF LEASE. At any time during the term of this Lease, either party, at its sole expense, shall be entitled to record a memorandum of this Lease and, if either party so elects, both parties agree to cooperate in the preparation, execution, acknowledgement and recordation of such document in reasonable form.

19.17 CORPORATE AUTHORITY. The- person signing this Lease on behalf of Tenant warrants that he or she is fully authorized to do so and, by so doing, to bind Tenant.

19.18 EXECUTION AND DELIVERY. This Lease may be executed in one or more counterparts and by separate parties on separate counterparts, but each such counterpart shall constitute an original and all such counterparts together shall constitute one and the same instrument.

19.19 SURVIVAL. Without limiting survival provisions which would otherwise be implied or construed under applicable law, the provisions of Sections 2.6, 7.4, 9.2, 9.3, 9.4, 11.6, 12.6 and 19.5 hereof shall survive the termination of this Lease with respect to matters occurring prior to the expiration of this Lease.

IN WITNESS WHEREOF, the parties hereto have executed this Lease as of the day and year first set forth above.

"Landlord"	"Tenant"
BRITANNIA POINTE GRAND LIMITED PARTNERSHIP, a Delaware limited partnership	RIGEL, INC., a Delaware corporation
By: BRITANNIA POINTE GRAND, LLC, a California limited liability company, General Partner	By: /s/ James M. Gower Its: CEO
By: /s/T. J. Bristow Its Manager, President and Chief Financial Officer	By: /s/ Brian C. Cunningham Its: Secretary

EXHIBITS

EXHIBIT A Real Property Description

EXHIBIT B Site Plan

EXHIBIT C Workletter

EXHIBIT D Estimated Construction Schedule

EXHIBIT E Acknowledgement of Rent Commencement Date

EXHIBIT A

REAL PROPERTY DESCRIPTION

All that certain real property in the City of South San Francisco, County of San Mateo, State of California, more particularly described as follows:

Lots 1, 2, 3 and 4, inclusive, as shown on Parcel Map No. 91-284, "Being a resubdivision of the parcels described in the deeds to Metal and Thermit Corporation, recorded in Book 293, at Page 394 of Deeds; in Book 49, at Page 490, Official Records; in Book 77, at Page 41:5, Official Records; and, except that parcel described in Book 1352, at Page 373, Official Records," filed on February 25, 1992, in Book 65 of Parcel Maps, in the Office of the Recorder of the County of San Mateo, California.

EXHIBIT B

SITE PLAN

[PLAN]

EXHIBIT C

WORKLETTER

This Workletter ("WORKLETTER") constitutes part of the Build-to-Suit Lease dated as of June 2, 1998 (the "LEASE") between BRITANNIA POINTE GRAND LIMITED PARTNERSHIP, a Delaware limited partnership ("LANDLORD"), and RIGEL, INC., a Delaware corporation ("TENANT"). The terms of this Workletter are incorporated in the Lease for all purposes.

1. DEFINED TERMS. As used in this Workletter, the following capitalized terms have the following meanings:

(a) APPROVED PLANS: Plans and specifications prepared by the applicable Architect for the respective Improvements and approved by both Landlord and Tenant in accordance with Paragraph 2 of this Workletter (subject to further modification in accordance with such Paragraph 2).

(b) ARCHITECT: Chamorro Design Group, or any other architect selected by Landlord in its sole discretion, with respect to the Building Shell, the Site Improvements and any other Improvements which Landlord is to design pursuant to this Workletter; any architect selected by Tenant with the written approval of Landlord (which approval shall not be unreasonably withheld or delayed), with respect to the Tenant Improvements and any other Improvements which Tenant is to design pursuant to this Workletter.

(c) BUILDING SHELL: The shell of the Building, as more fully defined in SCHEDULE C-1 attached to this Workletter.

(d) CHANGE ORDER: See definition in Paragraph 2(e)(ii) hereof.

(e) COST OF IMPROVEMENT: See definition in Paragraph 2(c) hereof.

(f) FINAL COMPLETION CERTIFICATE: See definition in Paragraph 3(0) hereof.

(g) FINAL WORKING DRAWINGS: See definition in Paragraph 2(a) hereof.

(h) GENERAL CONTRACTOR: Concrete Shell Structures, Inc., or any other general contractor selected by Landlord in its sole discretion, with respect to Landlord's Work. The General Contractor with respect to Tenant's Work shall be selected by Tenant, subject to Landlord's approval (not to be unreasonably withheld or delayed), as contemplated in Paragraph 5(a) hereof.

(i) IMPROVEMENTS: The Building Shell, Site Improvements, Tenant Improvements and other improvements shown on the Approved Plans from time to time and to be constructed on the Property pursuant to the Lease and this Workletter.

(j) LANDLORD DELAY: Any of the following types of delay in the completion of construction of the Tenant Improvements:

(i) Any delay resulting from Landlord's failure to furnish, in a timely manner, information requested by Tenant or by the Architect or General Contractor for Tenant's Work in connection with the design or construction of Tenant's Work, or from Landlord's failure to approve in a timely manner any matters requiring approval by Landlord; or

(ii) Any delay of any other kind or nature caused by Landlord (or Landlord's contractors, agents or employees) or resulting from the performance of Landlord's Work.

(k) LANDLORD'S WORK: The Building Shell and Site Improvements, and any other Improvements which Landlord is to construct or install pursuant to this Workletter or by mutual agreement of Landlord and Tenant from time to time.

(l) PUNCH LIST WORK: Minor corrections of construction or decoration details, and minor mechanical adjustments, that are required in order to cause any applicable portion of the Improvements as constructed to conform to the Approved Plans in all material respects and that do not materially interfere with Tenant's use or occupancy of the Building and the Property.

(m) SITE IMPROVEMENTS: The parking areas, driveways, landscaping and other improvements to the Common Areas of the Property that are depicted on EXHIBIT B to the Lease (as the same may be modified pursuant to the process of development and approval of the Approved Plans) and more specifically described in SCHEDULE C-1 attached to this Workletter.

(n) STRUCTURAL COMPLETION CERTIFICATE: See definition in Paragraph 3(a) hereof.

(o) TENANT DELAY: Any of the following types of delay in the completion of construction of the Building Shell:

(i) Any delay resulting from Tenant's failure to furnish, in a timely manner, information requested by Landlord or by the Architect or General Contractor for Landlord's Work in connection with the design or construction of the Building Shell, or from Tenant's failure to approve in a timely manner any matters requiring approval by Tenant;

(ii) Any delay attributable to any request by Tenant to construct the Building Shell in an "above standard" manner, or to any use of "above standard" Building Shell components that is necessitated by Tenant's particular use requirements or by the contemplated Tenant's Work;

(iii) Any delay resulting from Change Orders, including any delay resulting from the need to revise any drawings or obtain further governmental

approvals as a result of any Change Order; or

(iv) Any delay of any other kind or nature caused by Tenant (or Tenant's contractors, agents or employees) or resulting from the performance of Tenant's Work.

(p) TENANT IMPROVEMENTS: The improvements to or within the Building, other than improvements constituting pan of the Building Shell, shown on the Approved Plans from time to time and to be constructed by Tenant (except as otherwise provided herein) pursuant to the Lease and this Workletter, including (but not limited to) the improvements described on SCHEDULE C-2 attached to this Workletter (except to the extent any such SCHEDULE C-2 improvements constitute part of the Building Shell).

(q) TENANT'S WORK: All of the Improvements other than those constituting Landlord's Work, and such other materials and improvements as Tenant deems necessary or appropriate for Tenant's use and occupancy of the Building.

(r) UNAVOIDABLE DELAYS: Delays due to acts of God, acts of public agencies, labor disputes, strikes, fires, freight embargoes, rainy or stormy weather, inability to obtain supplies, materials, fuels or permits, delays of contractors or subcontractors, or other causes or contingencies beyond the reasonable control of Landlord or Tenant, as applicable.

(s) WORK DEADLINES: The target dates for performance by the applicable party of the steps listed in the Estimated Construction Schedule attached as EXHIBIT D to the Lease.

(t) Capitalized terms not otherwise defined in this Workletter shall have the definitions set forth in the Lease.

2. PLANS, COST OF IMPROVEMENTS AND CONSTRUCTION. Landlord and Tenant shall comply with the procedures set forth in this Paragraph 2 in preparing, delivering and approving matters relating to the Improvements.

(a) APPROVED PLANS AND WORKING DRAWINGS FOR LANDLORD'S WORK. Landlord shall promptly and diligently (and in all events prior to any applicable Work Deadlines, subject to Tenant Delays and Unavoidable Delays) cause to be prepared and delivered to Tenant, for approval, plans and specifications for the Improvements constituting Landlord's Work. Following mutual approval of such plans and specifications, Landlord shall then cause to be prepared and delivered to Tenant, on or before the applicable Work Deadline (assuming timely delivery by Tenant of all information, decisions and drawings required to be furnished or made by Tenant in order to permit complete preparation of plans and drawings), final working drawings and specifications for the Improvements constituting Landlord's Work, including structural, fire protection, life safety, mechanical and electrical working drawings and final architectural drawings (collectively, "LANDLORD'S FINAL WORKING DRAWINGS"). Landlord's Final Working Drawings shall substantially conform to the Approved Plans. Landlord's obligation to deliver Landlord's Final Working Drawings to Tenant within the time period set forth above shall be extended for any delay encountered by Landlord as a result of a request by Tenant for changes in accordance with the procedure set forth below, any other Tenant Delays, or any Unavoidable Delays. No later than the applicable Work Deadline (assuming timely delivery of plans and drawings by Landlord), Tenant shall either approve Landlord's Final Working Drawings or set forth in writing with particularity any changes necessary to bring Landlord's Final Working Drawings into substantial conformity with the Approved Plans or into a form which will be acceptable to Tenant. In no event, however, shall Tenant have the right to object to any aspect of the proposed plans and specifications or proposed Landlord's Final Working Drawings for Landlord's Work (including, but not limited to, any change from the Approved Plans) that is necessitated by applicable law, or to any aspect of such proposed plans and specifications or proposed Landlord's Final Working Drawings that relates to the Building Shell or Site Improvements, although Landlord agrees to consult with Tenant and to give reasonable consideration to Tenant's views regarding functional characteristics of the Building Shell and Site Improvements. Failure of Tenant to deliver to Landlord written notice of disapproval and specification of required changes on or before the applicable Work Deadline shall constitute and be deemed to be approval of Landlord's Final Working Drawings. Upon approval, actual or deemed, of Landlord's Final Working Drawings by Landlord and Tenant, Landlord's Final Working Drawings shall be deemed to be incorporated in and considered part of the Approved Plans, superseding (to the extent of any inconsistencies) any inconsistent features of the previously existing Approved Plans.

(b) APPROVED PLANS AND WORKING DRAWINGS FOR TENANT'S WORK. Tenant shall promptly and diligently (and in all events prior to any applicable Work Deadlines, subject to Landlord Delays and Unavoidable Delays) cause to be prepared and delivered to Landlord, for approval, plans and specifications for the Improvements constituting Tenant's Work. Following mutual approval of such plans and specifications, Tenant shall then cause to be prepared and

delivered to Landlord final working drawings and specifications for the Improvements constituting Tenant's Work, including any applicable life safety, mechanical and electrical working drawings and final architectural drawings (collectively, "TENANT'S FINAL WORKING DRAWINGS"). Tenant's Final Working Drawings shall substantially conform to the Approved Plans. Landlord shall either approve Tenant's Final Working Drawings or set forth in writing with particularity any changes necessary to bring Tenant's Final Working Drawings into substantial conformity with the Approved Plans or into a form which will be acceptable to Landlord. Upon approval of Tenant's Final Working Drawings by Landlord and Tenant, Tenant's Final Working Drawings shall be deemed to be incorporated in and considered part of the Approved Plans, superseding (to the extent of any inconsistencies) any inconsistent features of the previously existing Approved Plans.

(c) COST OF IMPROVEMENTS. "COST OF IMPROVEMENT" shall mean, with respect to any item or component for which a cost must be determined in order to allocate such cost, or an increase in such cost, to Landlord and/or Tenant pursuant to this Workletter, the sum of the following (unless otherwise agreed in writing by Landlord and Tenant with respect to any

specific item or component or any category of items or components): (i) all sums paid to contractors or subcontractors for labor and materials furnished in connection with construction of such item or component; (ii) all costs, expenses, payments, fees and charges (other than penalties) paid or incurred to or at the direction of any city, county or other governmental or quasi-governmental authority or agency which are required to be paid in order to obtain all necessary governmental permits, licenses, inspections and approvals relating to construction of such item or component; (iii) engineering and architectural fees for services rendered in connection with the design and construction of such item or component (including, but not limited to, the applicable Architect for such item or component and an electrical engineer, mechanical engineer and civil engineer); (iv) sales and use taxes; (v) testing and inspection costs; (vi) the cost of power, water and other utility facilities and the cost of collection and removal of debris required in connection with construction of such item or component; and (vii) all other "hard" costs incurred in the construction of such item or component in accordance with the Approved Plans and this Workletter. Cost of Improvement shall not include any project management fee relating to the construction of such item or component.

(d) CONSTRUCTION OF LANDLORD'S WORK. Promptly. following approval of Landlord's Final Working Drawings, Landlord shall apply for and use reasonable efforts to obtain the necessary permits and approvals to allow construction of all Improvements constituting Landlord's Work. Upon receipt of such permits and approvals, Landlord shall, at Landlord's sole expense (except as otherwise provided in the Lease or in this Workletter), diligently construct and complete the Improvements constituting Landlord's Work substantially in accordance with the Approved Plans, subject to Unavoidable Delays and Tenant Delays (if any). Such construction shall be performed in a neat and workmanlike manner and shall conform to all applicable governmental codes, laws and regulations in force at the time such work is completed. Landlord shall have the right, in its sole discretion, to decide whether and to what extent to use union labor on or in connection with Landlord's Work and shall use the General Contractor specified in Paragraph l(h) to construct all Improvements constituting Landlord's Work.

(e) CHANGES.

(i) If Landlord determines at any time that changes in Landlord's Final Working Drawings or in any other aspect of the Approved Plans relating to any item of Landlord's Work are required as a result of applicable law or governmental requirements, or at the insistence of any other third party whose approval, may be required with respect to the Improvements, or as a result of unanticipated conditions encountered in the course of construction, then Landlord shall promptly (A) advise Tenant of such circumstances and (B) cause revised Approved Plans and/or Landlord's Final Working Drawings, as applicable, reflecting such changes to be prepared by Architect and, to the extent such changes relate to items other than the Building Shell or Site Improvements, submitted to Tenant for approval in accordance with the procedure contemplated in Paragraph 2(a) hereof. Upon final approval of revised drawings by Landlord and Tenant (if applicable), Landlord's Final Working Drawings and/or Approved Plans shall be deemed to be modified accordingly.

(ii) If Tenant at any time desires any changes, alterations or additions to the Approved Plans or Landlord's Final Working Drawings with respect to any of Landlord's Work, Tenant shall submit a detailed written request to Landlord specifying such changes, alterations or additions (a "CHANGE ORDER"). Upon receipt of any such request, Landlord shall promptly notify Tenant of (A) whether the matters proposed in the Change Order are approved by Landlord (which approval shall not be unreasonably withheld), (B) Landlord's estimate of the number of days of delay, if any, which shall be caused by such Change Order if implemented (including, without limitation,

delays due to the need to obtain any revised plans or drawings and any governmental approvals), and (C) Landlord's estimate of the increase, if any, which shall occur in the Cost of Improvement for the items or components affected by such Change Order if such Change Order is implemented (including, but not limited to, any costs of compliance with laws or governmental regulations that become applicable because of the requested Change Order). If Tenant notifies Landlord in writing, within five (5) business days after receipt of such notice from Landlord, of Tenant's approval of the Change Order (including

the estimated delays and cost increases, if any, described in Landlord's notice), then Landlord shall cause Such Change Order to be implemented and Tenant shall be responsible for all costs or cost increases resulting from or attributable to the Change Order, subject to the provisions of Paragraph 4 hereof. If Tenant fails to notify Landlord in writing of Tenant's approval of such Change Order within said five (5) business day period, then such Change Order shall be deemed to be withdrawn and shall be of no further effect.

3. COMPLETION.

(a) When Landlord receives written certification from Architect that construction of the foundation, structural slab on grade, underslab plumbing work, structural steel framework, decking and concrete on second floor, roof structure and installation of main fire sprinkler lines in the Building have been completed in accordance with the Approved Plans, Landlord shall prepare and deliver to Tenant a certificate signed by both Landlord and Architect (the "STRUCTURAL COMPLETION CERTIFICATE") certifying that the construction of such portions of the Building has been substantially completed in accordance with the Approved Plans in all material respects and specifying the date of that completion. The delivery of such Structural Completion Certificate shall commence the running of the 6-month time period until the Rent Commencement Date under Section 2.1 of the Lease.

(b) When Landlord receives written certification from Architect that construction of the remaining Improvements constituting Landlord's Work has been completed in accordance with the Approved Plans (except for Punch List Work), Landlord shall prepare and deliver to Tenant a certificate signed by both Landlord and Architect (the "FINAL COMPLETION CERTIFICATE") certifying that the construction of the remaining Improvements constituting Landlord's Work has been substantially completed in accordance with the Approved Plans in all material respects, subject only to completion of Punch List Work, and specifying the date of that completion. Upon receipt by Tenant of the Final Completion Certificate, the Improvements constituting Landlord's Work will be deemed delivered to Tenant for all purposes of the Lease (subject to Landlord's continuing obligations with respect to the Punch List Work).

(c) Notwithstanding any other provisions of this Workletter or of the Lease, if Landlord is delayed in substantially completing any of Landlord's Work necessary for issuance of the Structural Completion Certificate as a result of any Tenant Delay, then the 6-month period between the delivery of the Structural Completion Certificate and the Rent Commencement Date pursuant to Section 2.1 of the Lease shall be reduced, day for day, by the number of days by which such Tenant Delay delayed completion of the portions of Landlord's Work necessary for issuance of the Structural Completion Certificate, and Tenant shall reimburse Landlord in cash, within fifteen (15) days after written demand by Landlord (accompanied by reasonable documentation of the items claimed), for any increased construction-related costs and expenses incurred by Landlord as a result of the Tenant Delay.

(d) At any time within thirty (30) days after delivery of the Structural Completion Certificate or the Final Completion Certificate, as applicable, Tenant shall be entitled to submit one or more lists to Landlord specifying Punch List Work to be performed on the applicable Improvements constituting Landlord's Work, and upon receipt of such list(s), Landlord shall diligently complete such Punch List Work at Landlord's sole expense. In the event of any dispute as to completion of any item or component of Landlord's Work, the certificate of the applicable Architect shall be conclusive. Promptly after Landlord provides Tenant with the Final Completion Certificate, Landlord shall cause the recordation of a Notice of Completion (as defined in Section 3093 of the California Civil Code) with respect to Landlord's Work.

4. PAYMENT OF COSTS.

(a) LANDLORD'S WORK. Except as otherwise expressly provided in this Workletter (including, but not limited to, the cost allocations set forth in SCHEDULE C-2 attached hereto) or by mutual written agreement of Landlord and Tenant, the cost of construction of Landlord's Work shall be borne by Landlord at its sole cost and expense, including any costs or cost increases incurred as a result of Unavoidable Delays, governmental requirements or

unanticipated conditions; PROVIDED, however, that notwithstanding any other provisions of this Paragraph 4(a), to the extent the Cost of Improvement relating to the construction of any item or component of Landlord's Work is increased as a result of any permitted Change Order or any Tenant Delay, or as a result of any "above standard" Building Shell components requested by Tenant or otherwise necessitated by Tenant's particular use requirements or by the contemplated Tenant's Work, or as a result of any other plan changes or compliance costs attributable to Tenant's particular use requirements or to the contemplated Tenant's Work, the amount of the increase in the Cost of Improvement with respect to such item or component shall be reimbursed by Tenant to Landlord in cash or, by mutual agreement of Landlord and Tenant, may be deducted from Landlord's maximum obligation under Paragraph 4(b) with respect to the cost of Tenant's Work.

(b) TENANT'S WORK. Except as otherwise expressly provided in this Workletter (including, but not limited to, the cost allocations set forth in SCHEDULE C-2 attached hereto) or by mutual written agreement of Landlord and Tenant, the cost of construction of the Tenant Improvements shall be borne eighty percent (80%) by Landlord and twenty percent (20%) by Tenant, up to a maximum Landlord's obligation of $115.00 per square foot of space in the Building (measured in accordance with Section 3.1(d) of the Lease), equating to a total Cost of Improvements for the Tenant Improvements of $143.75 per square foot. Tenant shall be responsible, at its sole cost and expense, for payment of twenty percent (20%) of the first $143.75 per square foot of the Cost of Improvements of the Tenant Improvements, for the entire Cost of Improvements of the Tenant Improvements in excess of $143.75 per square foot (if any such excess occurs) and for the entire cost of any Tenant's Work that is not part of the Tenant Improvements, including (but not limited to), in each case, any costs or cost increases incurred as a result of Unavoidable Delays, governmental requirements or unanticipated conditions. The rental schedule set forth in Section 3.1(a) of the Lease is NOT subject to adjustment based on the Cost of Improvements of the Tenant Improvements, regardless of whether the final Cost of Improvements for the Tenant Improvements uses the entire tenant improvement allowance of $115.00 per square foot that Landlord has agreed to make available as set forth above or is less than that amount. The timing, conditions and other procedures for payment or disbursement of Landlord's share of the cost of the Tenant Improvements (up to the maximum amount specified above) shall be subject to mutual agreement of Landlord, Tenant and Landlord's lender (if any). To the extent the Cost of Improvement with respect to the Tenant Improvements exceeds $143.75 per square foot (reduced by 125% of any amounts deducted from Landlord's maximum payment obligation as a result of the final sentence of Paragraph 4(a) hereof), whether as a result of Change Orders, Tenant Delays and/or Unavoidable Delays or otherwise, the amount of such excess shall in all events be Tenant's sole responsibility and expense.

5. TENANT'S WORK. On or before the applicable Work Deadline (subject to Landlord Delays and Unavoidable Delays, if any), Tenant shall construct and install in the Building the Tenant's Work, substantially in accordance with the Approved Plans or, with respect to Tenant's Work not shown on the Approved Plans, substantially in accordance with plans and specifications prepared by Tenant and approved in writing by Landlord (which approval shall not be unreasonably withheld or delayed). Tenant's Work shall be performed in accordance with, and shall in all respects be subject to, the terms and conditions of the Lease (to the extent not inconsistent with this Workletter), and shall also be subject to the following conditions:

(a) CONTRACTOR REQUIREMENTS. The contractor engaged by Tenant for Tenant's Work, and any subcontractors, shall be duly licensed in California and shall be subject to Landlord's prior written approval, which approval shall not be unreasonably withheld or delayed. Tenant shall engage only union contractors for the construction of Tenant's Work and for the installation of Tenant's fixtures and equipment in the Building, and shall require all such contractors engaged by Tenant, and all of their subcontractors, to use only union labor on or in connection with such work, except to the extent Landlord determines, in its reasonable discretion, that the use of non-union labor would not create a material risk of labor disputes, picketing or work interruptions at the Site, in which event Landlord shall, to that extent, waive such union labor requirement.

(b) COSTS AND EXPENSES OF TENANT'S WORK. Subject to Landlord's payment or reimbursement obligations under Paragraph 4(b) hereof with respect to Landlord's share of the Cost of Improvements for the Tenant Improvements, Tenant shall promptly pay all costs and expenses arising out of the performance of Tenant's Work (including the costs of permits) and shall furnish Landlord with evidence of payment on request. Tenant shall provide Landlord with ten (10) days' prior written notice before commencing any Tenant's Work. On completion of Tenant's Work, Tenant shall deliver to Landlord a release and waiver of lien executed by each contractor, subcontractor and materialman involved in the performance of Tenant's Work.

(c) INDEMNIFICATION. Tenant shall indemnify, defend (with counsel

satisfactory to Landlord) and hold Landlord harmless from all suits, claims, actions, losses, costs and expenses (including, but not limited to, claims for workers' compensation, attorneys' fees and costs) based on personal injury or property damage or contract claims (including, but not limited to, claims for breach of warranty) arising from the performance of Tenant's Work. Tenant shall repair or replace or, at Landlord's election, reimburse Landlord for the cost of repairing or replacing) any portion of the Improvements and/or any of Landlord's real or personal property or equipment that is damaged, lost or destroyed in the course of or in connection with the performance of Tenant's Work.

(d) INSURANCE. Tenant's contractors shall obtain and provide to Landlord certificates evidencing workers' compensation, public liability and property damage insurance in amounts and forms and with companies satisfactory to Landlord.

(e) RULES AND REGULATIONS. Tenant and Tenant's contractors shall comply with any other rules, regulations and requirements that Landlord or General Contractor may reasonably impose with respect to the performance of Tenant's Work. Tenant's agreement with Tenant's contractors shall require each contractor to provide daily cleanup of the construction area to the extent that such cleanup is necessitated by the performance of Tenant's Work.

(f) EARLY ENTRY. Landlord shall permit entry of contractors into the Building for the purposes of performing Tenant's Work, subject to satisfaction of the conditions set forth in the Lease. This license to enter is expressly conditioned on the contractor(s) retained by Tenant working in harmony with, and not interfering with, the workers, mechanics and contractors of Landlord. If at any time the entry or work by Tenant's contractor(s) causes any material interference with the workers, mechanics or contractors of Landlord, permission to enter may be withdrawn by Landlord immediately on written notice to Tenant.

(g) RISK OF LOSS. All materials, work, installations and decorations of any nature brought onto or installed in the Building, by or at the direction of Tenant or in connection with the performance of Tenant's Work, before the commencement of the Term shall be at Tenant's risk, and neither Landlord nor any party acting on Landlord's behalf shall be responsible for any damage, loss or destruction thereof.

(h) CONDITION OF TENANT'S WORK. All work performed by Tenant shall be performed in a good and workmanlike manner, shall be free from defects in design, materials and workmanship, and shall be completed in compliance with the plans approved by Landlord for such Tenant's Work in all material respects and in compliance with all applicable governmental laws, ordinances, codes and regulations in force at the time such work is completed.

6. NO AGENCY. Nothing contained in this Workletter shall make or constitute Tenant as the agent of Landlord.

7. SURVIVAL. Without limiting survival provisions which would otherwise be implied or construed under applicable law, the provisions of Paragraph 5(c) of this Workletter shall survive the termination of the Lease with respect to matters occurring prior to expiration of the Lease.

8. MISCELLANEOUS. All references in this Workletter to a number of days shall be construed to refer to calendar days, unless otherwise specified herein. In all instances where Tenant's approval is required, if no written notice of disapproval is given within the applicable time

period, at the end of that period Tenant shall be deemed to have given approval and the next succeeding time period shall commence. If any item requiring approval is disapproved by Tenant in a timely manner, the procedure for preparation of that item and approval shall be repeated.

IN WITNESS WHEREOF, the parties have executed this Workletter concurrently with and as of the date of the Lease.

"Landlord"	"Tenant"
BRITANNIA POINTE GRAND LIMITED PARTNERSHIP, a Delaware limited partnership	RIGEL, INC., a Delaware corporation
By: BRITANNIA POINTE GRAND, LLC, a California limited liability company, General Partner	By: /s/ James M. Gower James M. Gower Its: CEO
By: /s/ T. J. Bristow T. J. Bristow	By: /s/ Brian C. Cunningham

Its Manager, President and Chief Financial Officer

Its: Secretary

EXHIBIT E

ACKNOWLEDGEMENT OF RENT COMMENCEMENT DATE

This Acknowledgement is executed as of _____,1999, by BRITANNIA POINTE GRAND LIMITED PARTNERSHIP a Delaware limited partnership ("LANDLORD"), and RIGEL, INC., a Delaware corporation ("TENANT"), pursuant to Section 2.4 of the Build-to-Suit Lease dated June 2, 1998 between Landlord and Tenant (the "LEASE") covering premises located at _____, South San Francisco, CA 94080 (the "PROPERTY")

Landlord and Tenant hereby acknowledge and agree as follows:

1. The Rent Commencement Date under the Lease is _____, 1999.

2. The termination date under the Lease shall be _____ 2016, subject to any applicable provisions of the Lease for extension or early termination thereof.

3. The square footage of the Building, as finally designed and built, measured in accordance with Section 3.1(d) of the Lease, is _____ square feet.

4. Tenant accepts the Building and acknowledges the satisfactory completion of all Improvements therein required to be made by Landlord, subject only to (a) any applicable "punch list" or similar procedures specifically provided under the Lease or under the Workletter governing such work, and (b) Landlord's warranties and representations set forth in Section 5.2 of the Lease.

EXECUTED as of the date set forth above.

"Landlord"	"Tenant"
BRITANNIA POINTE GRAND LIMITED PARTNERSHIP, a Delaware limited partnership	RIGEL, INC., a Delaware corporation
By: BRITANNIA POINTE GRAND, LLC, a California limited liability company, General Partner	By:
By:	James M. Gower
T. J. Bristow	Its: CEO
Its Manager, President and Chief Financial Officer	By:
	Its:

EXHIBIT 23.1

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the reference to our firm under the captions "Selected Financial Data" and "Experts" and to the use of our report dated February 25, 2000, in the Registration Statement (Form S-1) and related Prospectus of Rigel Pharmaceuticals, Inc. for the registration of 10,350,000 shares of its common stock.

/s/ ERNST & YOUNG LLP

Palo Alto, California
September 15, 2000

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THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION EXTRACTED FROM UNAUDITED FINANCIAL STATEMENTS FOR THE SIX MONTH PERIODS ENDED JUNE 30, 1999 AND 2000 AND IS QUALIFIED IN ITS ENTIRETY BY REFERENCE TO SUCH FINANCIAL STATEMENTS.
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