AS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION ON SEPTEMBER 25, 2000

| | REGISTRATION NO. 333-44754 |
|---|--|
| | |
| SECURITIES AND EXCHANGE COM | MISSION |
| WASHINGTON, D.C. 2054 | 9 |
| AMENDMENT NO. 1 | |
| ТО | |
| FORM S-3 REGISTRATION STATEMEN | Т |
| UNDER THE SECURITIES ACT OF 1 | 933 |
| PROTEIN DESIGN LABS, IN (EXACT NAME OF REGISTRANT AS SPECIFIE | C. D IN ITS CHARTER) |
| DELAWARE | 94-3023969 |
| (STATE OR OTHER JURISDICTION OF INCORPORATION OR ORGANIZATION) | (I.R.S. EMPLOYE IDENTIFICATION NO |
| 34801 CAMPUS DRIVE FREMONT, CALIFORNIA 945 (510) 574-1400 (ADDRESS, INCLUDING ZIP CODE, AND TELEPHONE | |
| CODE, OF REGISTRANT'S PRINCIPAL EXE | |
| DOUGLAS O. EBERSOLE 34801 CAMPUS DRIVE FREMONT, CALIFORNIA 945 (510) 574-1400 | 55 |
| (NAME, ADDRESS, INCLUDING ZIP CODE, AND TELEPHONE OF AGENT FOR SERVICE) | |
| COPIES TO: | |
| GREGORY M. GALLO | ROD GUERRA, JR. |
| DOUGLAS J. REIN GRAY CARY WARE & FREIDENRICH LLP 400 HAMILTON AVENUE PALO ALTO, CALIFORNIA 94301 (650) 833-2000 | GREGORY C. SMITH SKADDEN, ARPS, SLATE, MEAGHER & FLOM LLP 525 UNIVERSITY AVE., SUITE 220 |
| APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED S practicable after this Registration Statement beco | |
| If the only securities being registered on thi pursuant to dividend or interest reinvestment plan pox: [] | |
| If any of the securities being registered on taled a delayed or continuous basis pursuant to Rule 415 1933, check the following box: [] | |
| If this Form is filed to register additional soursuant to Rule 462(b) under the Securities Act, and list the Securities Act registration statement effective registration statement for the same offe | please check the following box number of the earlier |
| If this Form is a post-effective amendment fil under the Securities Act, check the following box registration statement number of the earlier effec for the same offering. [] | and list the Securities Act |
| If delivery of the prospectus is expected to builder the Securities Act, please check the followi CALCULATION OF REGISTRATIO | ng box. [] |

| TITLE OF SECURITIES TO BE REGISTERED | AMOUNT TO BE REGISTERED | PROPOSED MAXIMUM AGGREGATE PRICE PER SHARE | PROPOSED MAXIMUM AGGREGATE OFFERING PRICE | AMOUNT OF REGISTRATION FEE |
|---|----------------------------|---|--|-------------------------------|
| Common Stock, \$.01 par value | 3,450,000 shares(1) | \$102.625(2) | \$354,056,250 | \$93,471(3) |
| | | | | |

- (1) Includes 450,000 shares which the Underwriters have the option to purchase to cover over allotments, if any.
- (2) Estimated solely for the purpose of computing the registration fee pursuant to Rule 457(c) and based on the average of the high and low sales prices on September 19, 2000 as reported on The Nasdaq Stock Market's National Market.
- (3) A registration fee of \$59,438 was previously paid.

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 WHICH 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 SUCH SECTION 8(A), MAY DETERMINE.

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.

SUBJECT TO COMPLETION, DATED SEPTEMBER 25, 2000

3,000,000 Shares

Protein Design Labs, Inc. Logo PROTEIN DESIGN LABS, INC.

Common Stock

Our common stock is listed on The Nasdaq Stock Market's National Market under the symbol "PDLI". The last reported sale price of our common stock on The Nasdaq Stock Market's National Market on September 22, 2000 was \$124.95 per share.

The underwriters have an option to purchase a maximum of 450,000 additional shares to cover overallotments of shares.

INVESTING IN OUR COMMON STOCK INVOLVES RISKS. SEE "RISK FACTORS" ON PAGE 6.

| | PRICE TO PUBLIC | UNDERWRITING DISCOUNTS AND COMMISSIONS | PROCEEDS TO PROTEIN DESIGN LABS |
|-----------|--------------------|--|---------------------------------|
| Per Share | \$ | \$ | \$ |
| Total | \$ | \$ | \$ |

Delivery of the shares of common stock will be made on or about , 2000.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

CREDIT SUISSE FIRST BOSTON

CIBC WORLD MARKETS

SG COWEN

The date of this prospectus is

, 2000.

PRODUCTS IN DEVELOPMENT

The following table summarizes the potential therapeutic indications, development status and commercial rights for our approved product and clinical product candidates and is qualified in its entirety by the more detailed information appearing elsewhere in this prospectus. Not all clinical trials being conducted are listed. The development and commercialization of our product candidates is subject to numerous risks and uncertainties. See "Risk Factors."

| ANTIBODY PRODUCT | INDICATION(S) | STATUS | |
|-----------------------------|------------------------------|--|--|
| Zenapax(R)(1) | Kidney transplant rejection | Marketed | |
| | Heart transplant rejection | Phase III | |
| | Psoriasis Uveitis | Phase II Phase I/II | |
| | Multiple sclerosis | Phase I/II | |
| SMART(TM) M195 | Acute myeloid leukemia | Phase III | |
| Nuvion(TM) | Psoriasis | Phase I/II | |
| | Transplantation | Phase II | |
| | Graft-versus-host disease | Phase I | |
| | Cutaneous T-cell lymphoma | Phase I | |
| SMART Anti-L-Selectin(2) | Trauma | Phase IIa | |
| SMART 1D10 | Non-Hodgkins B-cell lymphoma | Phase I | |
| Humanized Anti-IL-4(3) | Asthma | Phase I | |
| SMART Anti-Gamma Interferon | Autoimmune diseases | Phase I | |
| SMART Anti-VEGF(4) | Cancer | Phase I | |
| SMART Anti-E/P-Selectin | Stroke, asthma | Phase I in healthy volunteers complete | |

- (1) Hoffmann-La Roche Inc. and its affiliates (Roche) have marketing rights to Zenapax for transplantation. We share marketing rights with Roche for Zenapax's autoimmune indications.
- (2) Scil Biomedicals GmbH has European development and marketing rights to the SMART Anti-L-Selectin Antibody and is conducting the Phase IIa trial.
- (3) We licensed the humanized anti-IL-4 antibody from SmithKline Beecham Corporation, which has the option to acquire marketing rights after a specified Phase II trial and share development costs and profits from product sales.
- (4) We are developing the SMART Anti-VEGF Antibody with Toagosei Co., Ltd. Toagosei has marketing rights in Japan. We have marketing rights in North America and the option to market in the rest of the world outside of Japan.

Protein Design Labs, our logo and SMART are registered U.S. trademarks and Nuvion is a trademark of Protein Design Labs, Inc. Zenapax is a registered U.S. trademark of Roche. All other company names and trademarks included in this prospectus are trademarks, registered trademarks or trade names of their respective owners.

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YOU SHOULD RELY ONLY ON THE INFORMATION CONTAINED IN THIS DOCUMENT OR TO WHICH WE HAVE REFERRED YOU. WE HAVE NOT AUTHORIZED ANYONE TO PROVIDE YOU WITH INFORMATION THAT IS DIFFERENT. THIS DOCUMENT MAY ONLY BE USED WHERE IT IS LEGAL TO SELL THESE SECURITIES. THE INFORMATION IN THIS DOCUMENT MAY ONLY BE ACCURATE ON THE DATE OF THIS DOCUMENT.

We were incorporated in Delaware in 1986. Our principal executive offices are located at 34801 Campus Drive, Fremont, California 94555 and our phone number is (510) 574-1400. Our home page is www.pdl.com. Information contained on our Web site does not constitute part of this prospectus.

FORWARD-LOOKING STATEMENTS

This prospectus and the material incorporated by reference into this prospectus include "forward-looking statements" within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. All statements other than statements of historical facts are "forward-looking statements" for purposes of these provisions. These forward-looking statements include statements of the plans and objectives of management for future operations, statements concerning product development programs and clinical trials, statements regarding anticipated future economic conditions or performance, and statements of assumptions underlying any of the foregoing. In some cases, forward-looking statements are identified by the use of terminology such as "may", "will", "expects", "plans", "anticipates", "estimates", "potential", or "continue" or the negative thereof or other comparable terminology. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot assure you that those expectations or any of the forward-looking statements will prove to be correct, and actual results could differ materially from those projected or assumed in the forward-looking statements. Our future financial condition and results of operations, as well as any forward-looking statements, are subject to inherent risks and uncertainties, including but not limited to the risk factors set forth below, and for the reasons described elsewhere in this prospectus. All forward-looking statements and reasons why results may differ included in this prospectus are made as of the date hereof, and we assume no obligation to update these forward-looking statements or reasons why actual results might differ.

SUMMARY

This summary highlights information contained in other parts of this prospectus. Because it is a summary, it does not contain all of the information that you should consider before investing in the common stock. You should read the entire prospectus carefully.

PROTEIN DESIGN LABS, INC.

We are a leader in the development of humanized monoclonal antibodies for the prevention and treatment of disease. We have licensed rights to our first humanized antibody product, Zenapax, to Roche, which markets it for the prevention of kidney transplant rejection. We are also testing Zenapax for the treatment of autoimmune disease. In addition, we have eight other humanized antibodies in clinical development for autoimmune and inflammatory conditions, asthma and cancer.

We have fundamental patents in the U.S., Europe and Japan, which we believe cover most humanized antibodies. Eleven companies have licenses under these patents for humanized antibodies that they have developed. We receive royalties on sales of the three humanized antibodies developed by other companies that are currently being marketed.

THE OPPORTUNITY

During the past several years, there has been a resurgence of interest in the medical and commercial potential of monoclonal antibodies. The FDA has approved nine therapeutic antibodies, seven of them in the last three years, with total sales in 1999 in excess of \$1.0 billion. This resurgence has been made possible by the use of genetic engineering to create improved forms of antibodies. In particular, we developed and patented computer-aided technology to make humanized antibodies, which are antibodies that capture the benefits of traditional mouse-derived monoclonal antibodies while avoiding their limitations in treating humans.

Four of the nine therapeutic antibodies approved for marketing by the FDA are humanized antibodies, and at least 40 other humanized antibodies are currently in clinical trials. These humanized antibodies address many large markets, including cancer, stroke, heart disease, asthma, and autoimmune diseases such as psoriasis, multiple sclerosis and rheumatoid arthritis. A number of these antibodies have entered or completed the later phases of clinical development and, depending on satisfactory clinical results, may reach the marketplace in the next few years. As discussed further below, many of these antibodies are licensed under our patents, or are being developed by us.

In addition, with the sequencing of the human genome nearly complete, large numbers of new, potentially important therapeutic targets are being identified. Humanized antibodies can be routinely and reliably developed against almost any cell surface or extracellular target. Hence, we believe that humanized antibodies will be a key part of the next generation of pharmaceutical products.

STRATEGY

Our objective is to leverage our product pipeline and patent portfolio in the field of antibodies to become a fully-integrated, profitable, research-based biopharmaceutical company. We derive revenues, and expect to derive revenues in the future, from three major sources:

- Sales of products that we have developed. We receive royalties on sales of Zenapax by our licensee, Roche. We have eight other humanized antibodies in clinical development. We plan to market some of our products, once approved, in North America, especially for specialty markets such as cancer that we believe can be effectively serviced with a relatively small sales force. We may license marketing rights for some antibodies or some geographic areas to other pharmaceutical companies.
- Royalties from the sale of humanized antibodies developed by other companies. We license our patents covering humanized antibodies in return for license fees, annual maintenance payments and

royalties on product sales. The three humanized antibodies currently approved by the FDA in addition to Zenapax are licensed under our patents. Two of these antibodies are Genentech's Herceptin and MedImmune's Synagis, which had reported sales totaling approximately \$480 million in 1999 and on which we are currently receiving royalties. The third is American Home Products' Mylotarg, which it began marketing in May 2000. We have license agreements with eight other companies for humanized antibodies they are developing.

- Research and development contracts with other companies. We humanize antibodies for other companies in return for upfront fees, milestone payments and royalties on any product sales. In some cases we also receive the right to co-promote these products in designated territories. We also sometimes license out marketing rights to a humanized antibody that we are developing, and then typically receive upfront fees and milestone payments and/or research funding, in addition to royalties on any product sales by our licensee.

PRODUCTS IN DEVELOPMENT

We have the following products under clinical development. We usually refer to the humanized antibodies that we have made as SMART antibodies.

- Zenapax. The FDA approved Zenapax in December 1997 for the prevention of kidney transplant rejection. Zenapax was the first humanized antibody to be approved anywhere in the world. Our licensee Roche sells this product in the U.S., Europe and other territories for the transplant indication. Zenapax works by blocking the activation of T cells, which play a key role in both transplant rejection and autoimmune disease. Zenapax is the first effective immunosuppressive drug without significant side effects. As a result, we believe Zenapax may be useful for the long-term treatment of autoimmune diseases such as psoriasis and multiple sclerosis. In 1999, we reacquired from Roche specific development and marketing rights to Zenapax for autoimmune diseases.

Zenapax is currently in two Phase II trials in psoriasis, a common autoimmune disease of the skin, and in early stage trials for uveitis, multiple sclerosis, aplastic anemia, and the ocular manifestations of Bechet's disease. We plan to conduct additional trials for psoriasis and other autoimmune diseases. In the early stage clinical trial for uveitis, an autoimmune disease of the eye, Zenapax was safely administered to patients for one year and was effective in controlling the disease in most patients, some of whom have continued to receive Zenapax for up to three years.

- SMART M195 Antibody. This antibody has completed a Phase II trial and is now in a Phase III trial for the treatment of acute myeloid leukemia, a disease that has approximately 10,000 new cases in the U.S. each year and has a high mortality rate. An interim review of the trial results by an independent data safety monitoring board is expected in the fourth quarter of 2000. The monitoring board could recommend or require that the trial be terminated if the interim data do not show a sufficient probability of the trial being successful or if specified safety criteria are not met. If the final results of the trial are positive, we expect to file for marketing approval.
- Nuvion (SMART Anti-CD3 Antibody). We are developing this antibody for the treatment of autoimmune diseases. Although both Nuvion and Zenapax may target some of the same diseases, we believe they may have complementary roles in medical treatment. Nuvion may be more potent than Zenapax, but may not be suitable for chronic administration, so it may be most useful to treat acute episodes of autoimmune disease and to induce remissions. Zenapax may be useful to maintain the remissions for longer periods. Nuvion is currently in a Phase I/II clinical trial for psoriasis. It is also in clinical trials for transplant rejection, graft-versus-host disease, and cutaneous T-cell lymphoma, but we have no current plans to conduct Phase III trials in these indications.
- SMART Anti-L-Selectin Antibody. This antibody may be useful for preventing the multiple organ failure and mortality that often follows severe trauma. In 1999, we licensed European marketing rights for this antibody to Scil Biomedicals. Scil paid us a licensing fee and agreed to conduct and pay for clinical trials in Europe and to provide us with the data; in return, we are making milestone

payments to Scil on the achievement of defined clinical and regulatory goals. Scil has completed a Phase I trial of SMART Anti-L-Selectin and is now conducting a Phase IIa trial for treatment of trauma. If the results from that Phase IIa trial are encouraging, we may initiate clinical development in the U.S.

- SMART 1D10 Antibody. The National Cancer Institute is sponsoring a Phase I trial of this antibody for non-Hodgkins B-cell lymphoma. Clinical responses were observed in three of the patients in this trial, and we plan to initiate a Phase II trial. SMART 1D10 is directed to a different target on B cells than Rituxan, the antibody currently marketed for non-Hodgkins lymphoma, and thus may provide an alternative therapy. In the U.S., approximately 290,000 patients have this disease and 55,000 new cases occur annually.
- Humanized Anti-IL-4 Antibody. We licensed this antibody, for the potential treatment of asthma and allergy, from SmithKline in 1999. The humanized anti-IL-4 antibody blocks the effects of interleukin 4, which is believed to play a key role in initiating the series of biological processes that lead to allergy and asthma. SmithKline began a Phase I trial of the humanized anti-IL-4 antibody, which we have now completed. We plan to initiate a Phase I/II multiple dose study, followed by a Phase II trial in moderate to severe asthma patients.
- SMART Anti-Gamma Interferon Antibody. This antibody targets gamma interferon, a protein that stimulates several types of white blood cells and that may be involved in some autoimmune diseases. We have completed a Phase I trial of SMART Anti-Gamma Interferon in normal volunteers, which showed the antibody is well-tolerated and has biological activity. We plan to initiate a Phase I/II trial in patients with Crohn's disease, a form of inflammatory bowel disease. In the future, we may initiate clinical trials in other autoimmune diseases.
- SMART Anti-VEGF Antibody. This antibody blocks the action of vascular endothelial growth factor (VEGF), which is believed to play an important role in the formation of blood vessels in tumors, a process that allows the tumors to grow. We humanized the antibody for Toagosei, a Japanese chemical company, and subsequently entered into an agreement with Toagosei under which the two companies will share development costs, marketing rights, and profits from potential sales of the antibody in markets outside of Japan. We are currently conducting a Phase I trial of the antibody in collaboration with the European Organization for Research and Treatment of Cancer.
- SMART Anti-E/P-Selectin Antibody. This antibody targets adhesion molecules on the inside of blood vessels that may be involved in inflammation. We have completed a Phase I trial of SMART Anti-E/P-Selectin in healthy volunteers, which showed that the antibody is well-tolerated in a range of doses. We have retained worldwide rights to SMART Anti-E/P-Selectin and are seeking a partner for its further development.

RECENT DEVELOPMENTS

Our patents for humanized antibodies are being opposed in patent office proceedings in Europe and Japan, and a successful challenge could limit our future revenues from licensing these patents. At an oral hearing on March 20, 2000, the Opposition Division of the European Patent Office decided to revoke the broad claims in our first European patent pertaining generally to antibody humanization. We plan to appeal this decision to the Technical Board of Appeal of the European Patent Office.

On March 28, 2000, we granted a license under our humanization patents to Merck KGaA, an international pharmaceutical company based in Germany, for an antibody they are developing. We received a signing and licensing fee and are entitled to royalties on any product sales.

On May 8, 2000, we granted multiple licenses under our humanization patents to Chugai Pharmaceutical Company. We received a signing and licensing fee of \$6.0 million and are entitled to royalties on any product sales.

On August 30, 2000 and September 15, 2000, we entered into two agreements to humanize antibodies for Eli Lilly and Company. Lilly agreed to pay us signing and licensing fees of \$1.7 million and \$1.36 million and to make additional payments upon the achievement of specified milestones and to pay royalties on any sales of the humanized antibodies.

THE OFFERING

Common stock offered.......... 3,000,000 shares

Common stock outstanding after

the offering...... 42,849,124 shares

Use of proceeds...... To fund clinical trials, to expand

manufacturing capabilities, to expand our marketing and sales capabilities, and for working capital and other general corporate

purposes.

Nasdaq National Market

symbol..... PDLI

The number of shares of our common stock to be outstanding after this offering is based on the number of shares outstanding as of June 30, 2000 and excludes as of that date:

- 5,227,090 shares issuable upon exercise of outstanding stock options with a weighted average exercise price of \$21.98 per share, of which options to purchase 1,463,383 were then exercisable
- 2,539,348 shares available for future option grants under our stock option plan
- 730,608 shares available for sale under our employee stock purchase plan, and
- 1,986,755 shares issuable on conversion of our outstanding convertible notes.

All information in this prospectus has been adjusted to give effect to the increase in our authorized shares of common stock effected in July 2000 and the two-for-one split of our common stock effected on August 23, 2000.

SUMMARY FINANCIAL DATA

(IN THOUSANDS, EXCEPT PER SHARE DATA)

| | YEARS EI | NDED DECEMBI | SIX MONTHS ENDED JUNE 30, | | |
|---|-----------|--------------|------------------------------|-----------|----------|
| | 1997 1998 | | 1999 | 1999 | 2000 |
| | | | | (UNAUD | ITED) |
| SUMMARY OF OPERATIONS DATA: | | | | | |
| Total revenues | \$ 20,255 | \$30,828 | \$ 35,754 | \$17,124 | \$35,864 |
| Net income (loss) Net income (loss) per share: | (23,875) | (9,502) | (10,333) | (4,564) | 5,791 |
| Basic | \$ (0.68) | \$ (0.26) | \$ (0.28) | \$ (0.12) | \$ 0.15 |
| Diluted | \$ (0.68) | \$ (0.26) | \$ (0.28) | \$ (0.12) | \$ 0.13 |
| Weighted average number of shares: | , , | ` , | ` , | , , | |
| Basic | 35,298 | 37,050 | 37,396 | 37,244 | 39,218 |
| Diluted | 35, 298 | 37,050 | 37, 396 | 37,244 | 43, 186 |

| | | NE 30, 2000 |
|--|--|--|
| | ACTUAL | |
| | (UNA | UDITED) |
| BALANCE SHEET DATA: Cash, cash equivalents and investments Working capital Total assets Long-term debt, excluding current maturities Convertible debt Total stockholders' equity | \$309,881 194,468 354,658 9,527 150,000 185,670 | \$665,489 550,076 710,266 9,527 150,000 541,278 |

The as adjusted column reflects our receipt of the estimated net proceeds from the sale of the 3,000,000 shares of common stock offered in this offering at an assumed public price of \$124.95 per share, and after deducting the estimated discount and estimated offering expenses payable by us.

RISK FACTORS

An investment in our common stock is very risky. You should carefully consider the factors described below in addition to the other information in this prospectus before purchasing our shares. Additional risks and uncertainties not presently known to us or that we currently see as immaterial may also impair our business. If any of these risks actually occurs, it could materially harm our business, financial condition or operating results. In that case, the price of our common stock could decline and you may lose part or all of your investment.

RISKS RELATING TO OUR COMPANY

WE HAVE A HISTORY OF OPERATING LOSSES AND MAY NOT ACHIEVE SUSTAINED PROFITABILITY.

Our expenses have generally exceeded revenues. As of June 30, 2000, we had an accumulated deficit of approximately \$73.4 million. We believe that our losses may increase because of the extensive resource commitments required to achieve regulatory approval and commercial success for any individual product. For example, over the next several years, we will incur substantial additional expenses as we continue to develop and manufacture our potential products, invest in new research areas and improve and expand our manufacturing, marketing and sales capabilities. Since we or our collaborative partners or licensees may not be able to successfully develop additional products, obtain required regulatory approvals, manufacture products at an acceptable cost and with appropriate quality, or successfully market such products with desired margins, we may never achieve sustained profitable operations. The amount of net losses and the time required to reach sustained profitability are highly uncertain. We may be unable to achieve or sustain profitability.

Our commitment of resources to the continued development of our products will require significant additional funds for development. Our operating expenses may also increase as:

- some of our earlier stage potential products move into later stage clinical development
- additional potential products are selected as clinical candidates for further development
- we invest in additional manufacturing capacity
- we defend or prosecute our patents and patent applications, and
- we invest in research or acquire additional technologies, product candidates or businesses.

In the absence of substantial revenues from new corporate collaborations or patent licensing or humanization agreements, significant royalties on sales of products licensed under our intellectual property rights, product sales or other uncertain sources of revenue, we will incur substantial operating losses.

OUR REVENUES, EXPENSES AND OPERATING RESULTS WILL LIKELY FLUCTUATE IN FUTURE PERIODS.

Our revenues have varied in the past and will likely continue to fluctuate considerably from quarter to quarter and from year to year. As a result, our revenues in any period may not be predictive of revenues in any subsequent period. Our royalty revenues may be unpredictable and may fluctuate since they depend upon:

- the seasonality of sales of licensed products
- the existence of competing products
- the marketing efforts of our licensees
- potential reductions in royalties payable to us due to credits for prior payments to us
- the timing of royalty reports, some of which are required quarterly and others semi-annually

- our method of accounting for royalty revenues from our licensees, and
- our ability to successfully defend and enforce our patents.

Other revenue may also be unpredictable and may fluctuate due to the timing of payments of non-recurring licensing and signing fees and payments for manufacturing services and achievement of milestones under new and existing collaborative, humanization, and patent licensing agreements. Revenue historically recognized under our prior agreements may not be an indicator of non-royalty revenue from any future collaborations.

In addition, our expenses may be unpredictable and may fluctuate from quarter to quarter due to the timing of expenses, which may include payments owed by us under licensing arrangements and due to our policy of recording expenses under certain collaborative agreements during the quarter in which such expenses are reported to us.

In the second quarter of 2000, we received \$20.4 million in revenue. This included \$6.5 million in non-recurring revenue from our multiple patent licenses with Chugai and from expansion of a patent license with American Home Products. To date in the third quarter of 2000, we have entered into two new humanization agreements, and we cannot predict the amount of revenue, if any, that will be derived from these or any other new agreements in the quarter. We also received significant royalty revenues on sales of the product Synagis in the second quarter. This product has higher sales in the fall and winter, which to date have resulted in much higher royalties paid to us in our first and second quarters than in other quarters. We expect to receive approximately \$5.0 million less in revenue from Synagis royalties in the third quarter than in the second quarter of 2000 and aggregate royalties from sales of other products to be roughly comparable to those in the second quarter. As a result of these factors, we expect both royalty and non-royalty revenues in both the third and fourth quarters of 2000 to be significantly below their levels for the second quarter. In addition, we expect to incur losses in the third and fourth quarters that will exceed in the aggregate the income we earned for the first half of 2000.

OUR HUMANIZATION PATENTS ARE BEING OPPOSED AND A SUCCESSFUL CHALLENGE COULD LIMIT OUR FUTURE REVENUES.

Substantially all of our current revenues are related to our humanization patents. At an oral hearing in March 2000, the Opposition Division of the European Patent Office decided to revoke the broad claims of our first European humanization patent. We plan to appeal this decision and until our appeal is resolved, we may be limited in our ability to collect royalties or to negotiate future licensing or collaborative research and development arrangements based on this and our other humanization patents. Moreover, if our appeal is unsuccessful, our ability to collect royalties on European sales of antibodies humanized by others would depend on the scope and validity of our second European patent, whether the antibodies are manufactured in a country outside of Europe where they are covered by one of our patents, and in that case the terms of our license agreements with respect to that situation. Also, the Opposition Division's decision could encourage challenges of our related patents in other jurisdictions, including the U.S. This decision may lead some of our licensees to stop making royalty payments or lead potential licensees not to take a license, either of which might result in us initiating formal legal actions to enforce our rights under our humanization patents. In such a situation, a likely defensive strategy to our action would be to challenge our patents in that jurisdiction. During the appeals process with respect to our first European patent, if we were to commence an infringement action to enforce that patent, such an action would likely be stayed until the appeal is decided by the European Patent Office. As a result, we may not be able to successfully enforce our rights under our European or related U.S. and Japanese patents. We have been advised that eight notices of opposition have been filed with respect to our second European antibody humanization patent. Also, three opposition statements have been filed with the Japanese Patent Office with respect to our humanization patent issued in Japan in late 1998.

We intend to vigorously defend the European patents and the Japanese patent in these proceedings; however, we may not prevail in the opposition proceedings or any litigation contesting the validity of these patents. If our appeal with respect to our first European patent is unsuccessful or if the outcome of the other European or Japanese opposition proceedings or any litigation involving our antibody humanization

patents were to be unfavorable, our ability to collect royalties on existing licensed products and to license our patents relating to humanized antibodies may be materially harmed. In addition, these proceedings or any other litigation to protect our intellectual property rights or defend against infringement claims by others could result in substantial costs and diversion of management's time and attention, which could harm our business and financial condition.

IF WE ARE UNABLE TO PROTECT OUR PATENTS AND PROPRIETARY TECHNOLOGY, WE MAY NOT BE ABLE TO COMPETE SUCCESSFULLY.

Our pending patent applications may not result in the issuance of valid patents or our issued patents may not provide competitive advantages. Also, our patent protection may not prevent others from developing competitive products using related or other technology.

A number of companies, universities and research institutions have filed patent applications or received patents in the areas of antibodies and other fields relating to our programs. Some of these applications or patents may be competitive with our applications or contain material that could prevent the issuance of patents to us or result in a significant reduction in the scope of our issued patents.

The scope, enforceability and effective term of patents can be highly uncertain and often involve complex legal and factual questions. No consistent policy has emerged regarding the breadth of claims in biotechnology patents, so that even issued patents may later be modified or revoked by the relevant patent authorities or courts. Moreover, the issuance of a patent in one country does not assure the issuance of a patent with similar claims in another country, and claim interpretation and infringement laws vary among countries, so we are unable to predict the extent of patent protection in any country.

In addition to seeking the protection of patents and licenses, we also rely upon trade secrets, know-how and continuing technological innovation which we seek to protect, in part, by confidentiality agreements with employees, consultants, suppliers and licensees. If these agreements are not honored, we might not have adequate remedies for any breach. Additionally, our trade secrets might otherwise become known or patented by our competitors.

WE MAY REQUIRE ADDITIONAL PATENT LICENSES IN ORDER TO MANUFACTURE OR SELL OUR POTENTIAL PRODUCTS.

Other companies, universities and research institutions may obtain patents that could limit our ability to use, import, manufacture, market or sell our products or impair our competitive position. As a result, we might be required to obtain licenses from others before we could continue using, importing, manufacturing, marketing, or selling our products. We may not be able to obtain required licenses on terms acceptable to us, if at all. If we do not obtain required licenses, we may encounter significant delays in product development while we redesign potentially infringing products or methods or may not be able to market our products at all.

Celltech Therapeutics Limited has been granted a European patent covering humanized antibodies, which we have opposed. At an oral hearing in September 2000, the Opposition Division of the European Patent Office decided to revoke this patent. Celltech may elect to appeal that decision. Also, Celltech has a pending divisional patent application in Europe, which is currently drafted with broad claims directed towards humanized antibodies. We cannot predict whether Celltech will be able to successfully appeal the decision of the Opposition Division with respect to their first European patent or whether they will be able to obtain the grant of a patent from the pending application with claims broad enough to generally cover humanized antibodies. Celltech has also been issued a corresponding U.S. patent that contains claims that may be considered broader in scope than their first European patent. We have entered into an agreement with Celltech providing each company with the right to obtain nonexclusive licenses for up to three antibody targets under the other company's humanization patents. Nevertheless, if our SMART antibodies were covered by Celltech's European or U.S. patents and if we were to need more than the three licenses under those patents currently available to us under the agreement, we would be required to negotiate additional licenses under those patents or to significantly alter our processes or products. We might not be

able to successfully alter our processes or products to avoid conflict with these patents or to obtain the required additional licenses on commercially reasonable terms, if at all.

In addition, if the Celltech U.S. patent or any related patent applications conflict with our U.S. patents or patent applications, we may become involved in proceedings to determine which company was the first to invent the products or processes contained in the conflicting patents. These proceedings could be expensive, last several years and either prevent issuance of additional patents to us relating to humanization of antibodies or result in a significant reduction in the scope or invalidation of our patents. Any limitation would reduce our ability to negotiate or collect royalties or to negotiate future collaborative research and development agreements based on these patents.

Lonza Biologics, Inc. has a patent issued in Europe to which we do not have a license that may cover a process that we use to produce our potential products. In addition, we do not have a license to an issued U.S. patent assigned to Stanford University and Columbia University, which may cover a process we use to produce our potential products. We have been advised that an exclusive license has been previously granted to a third party under this patent. If our processes were covered by either of these patents, we might be required to obtain licenses or to significantly alter our processes or products. We might not be able to successfully alter our processes or products to avoid conflicts with these patents or to obtain licenses on acceptable terms.

Toagosei Co., Ltd. is subject to a claim alleging patent infringement based on the importation into the U.S. by Toagosei to us of an antibody alleged to have been analyzed in violation of a third party's patents directed to an animal model. To date, we have not directly been made subject to such a claim and, although we are still investigating the matter, we have reached a preliminary conclusion that these allegations lack merit. We cannot, however, assure you that our preliminary conclusion would be found to be correct. The third party has made a settlement offer to Toagosei, which even if agreed to and shared by us (although we may be entitled to indemnification), would not materially affect our financial condition. Nevertheless, we cannot assure you that these allegations can be settled on reasonable terms, if at all.

IF WE CANNOT SUCCESSFULLY COMPLETE OUR CLINICAL TRIALS, WE WILL BE UNABLE TO OBTAIN REGULATORY APPROVALS REQUIRED TO MARKET OUR PRODUCTS.

To obtain regulatory approval for the commercial sale of any of our potential products or to promote these products for expanded indications, we must demonstrate through preclinical testing and clinical trials that each product is safe and effective for use in indications for which approval is requested. We have conducted only a limited number of clinical trials to date. We may not be able to successfully commence and complete all of our planned clinical trials without significant additional resources and expertise. Our potential inability to commence or continue clinical trials, to complete the clinical trials on a timely basis or to demonstrate the safety and efficacy of our potential products, further adds to the uncertainty of regulatory approval for our potential products.

Larger and later stage clinical trials may not produce the same results as early stage trials. Many companies in the pharmaceutical and biotechnology industries, including our company, have suffered significant setbacks in clinical trials, including advanced clinical trials, even after promising results had been obtained in earlier trials.

Even when a drug candidate shows indications of efficacy in a clinical trial, it may be impossible to further develop or receive regulatory approval for the drug if it causes an unacceptable incidence or severity of side effects, or further development may be slowed down by the need to find dosing regimens that do not cause such side effects. For example, while Nuvion has shown biological activity in some patients in the Phase I/II trial for psoriasis, it has also at some dose levels caused a level of side effects that would be unacceptable in this patient population. Hence, we plan to conduct a Phase II trial of Nuvion in psoriasis in an attempt to find a dosing regimen that is both well-tolerated and effective. However, we may not be able to find such a regimen, and inability to do so would prevent further development of Nuvion for the psoriasis indication. As a second example, the SMART 1D10 Antibody produced partial clinical responses in some B-cell lymphoma patients but at some dose levels there were

significant side effects. Hence, we plan to conduct a Phase II trial of SMART 1D10 to determine the optimum dosing regimen.

OUR CLINICAL TRIAL STRATEGY MAY INCREASE THE RISK OF CLINICAL TRIAL DIFFICULTIES.

Research, preclinical testing and clinical trials may take many years to complete and the time required can vary depending on the indication being addressed and the nature of the product. We may at times elect to use aggressive clinical strategies in order to advance potential products through clinical development as rapidly as possible. For example, we may commence clinical trials without conducting preclinical animal efficacy testing, where an appropriate animal efficacy testing model does not exist, or we may conduct later stage trials based on limited early stage data. As a result, we anticipate that only some of our potential products may show safety and efficacy in clinical trials and some may encounter difficulties or delays during clinical development.

For example, we have entered the SMART M195 Antibody into a Phase III clinical trial in acute myelogenous leukemia with a clinical regimen that has not been tested previously with this antibody in combination with chemotherapy. Results from our prior Phase II and Phase II/III studies showed only a limited number of complete and partial remissions using the antibody without concomitant chemotherapy. In addition, based in part on the nature and severity of the disease, we initiated a Phase III study without a meeting with the FDA or European regulatory authorities to discuss the protocol and its adequacy to support approval of the SMART M195 Antibody. This study may not be successful, or the FDA or European regulatory authorities may not agree that the study will be adequate to obtain regulatory approval, even if the study is successful. In addition, the protocol for our Phase III trial includes an interim review by an independent data safety monitoring board, which we expect to take place in the fourth quarter of 2000. The monitoring board could recommend or require that the trial be terminated if the interim data do not show a sufficient probability of the trial being successful or if specified safety criteria are not met.

WE MAY BE UNABLE TO ENROLL SUFFICIENT PATIENTS TO COMPLETE OUR CLINICAL TRIALS.

The rate of completion of our clinical trials, and those of our collaborators, is significantly dependent upon the rate of patient enrollment. Patient enrollment is a function of many factors, including:

- the size of the patient population
- perceived risks and benefits of the drug under study
- availability of competing therapies
- availability of clinical drug supply
- availability of clinical trial sites
- design of the protocol
- proximity of and access by patients to clinical sites
- patient referral practices of physicians
- eligibility criteria for the study in question, and
- efforts of the sponsor of and clinical sites involved in the trial to facilitate timely enrollment.

We may have difficulty obtaining sufficient patient enrollment or clinician support to conduct our clinical trials as planned, and we may need to expend substantial additional funds to obtain access to resources or delay or modify our plans significantly. These considerations may lead us to consider the termination of ongoing clinical trials or development of a product for a particular indication.

OUR REVENUES FROM LICENSED TECHNOLOGIES DEPEND ON THE EFFORTS AND SUCCESSES OF OUR LICENSEES.

In those instances where we have licensed rights to our technologies, the product development and marketing efforts and successes of our licensees will determine the amount and timing of royalties we may receive, if any. We have no assurance that any licensee will successfully complete the product development, regulatory and marketing efforts required to sell products. The success of products sold by licensees will be affected by competitive products, including potential competing therapies that are marketed by the licensee or others.

IF OUR COLLABORATIONS ARE NOT SUCCESSFUL, WE MAY NOT BE ABLE TO EFFECTIVELY DEVELOP AND MARKET SOME OF OUR PRODUCTS.

We have collaborative agreements with several pharmaceutical and other companies to develop, manufacture and market Zenapax and some of our potential products. In some cases, we are relying on our collaborative partners to manufacture such products, to conduct clinical trials, to compile and analyze the data received from these trials, to obtain regulatory approvals and, if approved, to market these licensed products. As a result, we may have little or no control over the manufacturing, development and marketing of these potential products and little or no opportunity to review clinical data prior to or following public announcement.

Our collaborative agreements can generally be terminated by our partners on short notice. A collaborator may terminate its agreement with us or separately pursue alternative products, therapeutic approaches or technologies as a means of developing treatments for the diseases targeted by us or our collaborative effort. Even if a collaborator continues its contributions to the arrangement, it may nevertheless determine not to actively pursue the development or commercialization of any resulting products. In these circumstances, our ability to pursue potential products could be severely limited.

Continued funding and participation by collaborative partners will depend on the timely achievement of our research and development objectives, the retention of key personnel performing work under those agreements and on each collaborative partner's own financial, competitive, marketing and strategic considerations. Such considerations include:

- the commitment of management of the collaborative partners to the continued development of the licensed products or technology
- the relationships among the individuals responsible for the implementation and maintenance of the collaborative efforts, and
- the relative advantages of alternative products or technology being marketed or developed by the collaborators or by others, including their relative patent and proprietary technology positions, and their ability to manufacture potential products successfully.

Our ability to enter into new collaborations and the willingness of our existing collaborators to continue development of our potential products depends upon, among other things, our patent position with respect to such products. If we are unable to successfully maintain our patents we may be unable to collect royalties on existing licensed products or enter into additional collaborations and agreements.

IMPLEMENTATION OF STAFF ACCOUNTING BULLETIN NO. 101 MAY REQUIRE US TO REVISE OUR FINANCIAL STATEMENTS OR OUR REVENUE RECOGNITION PRACTICES.

In December 1999, the SEC issued Staff Accounting Bulletin No. 101, "Revenue Recognition in Financial Statements" (SAB 101). We are evaluating the effects, if any, that the adoption of SAB 101 in the fourth quarter of 2000, effective January 1, 2000, may have on the results of our operations or our financial position. We have been advised that the SEC intends to provide additional guidance during the third quarter of 2000 with respect to the implementation of SAB 101. We do not know whether this guidance and implementation of SAB 101 will require us to revise our revenue recognition practices or to restate revenues for the first and second quarters of 2000.

OUR LACK OF EXPERIENCE IN SALES, MARKETING AND DISTRIBUTION MAY HAMPER MARKET INTRODUCTION AND ACCEPTANCE OF OUR PRODUCTS.

We intend to market and sell a number of our products either directly or through sales and marketing partnership arrangements with collaborative partners. To market products directly, we must either establish a marketing group and direct sales force or obtain the assistance of another company. We may not be able to establish marketing, sales and distribution capabilities or succeed in gaining market acceptance for our products. If we were to enter into co-promotion or other marketing arrangements with pharmaceutical or biotechnology companies, our revenues would be subject to the payment provisions of these arrangements and dependent on the efforts of third parties.

MANUFACTURING DIFFICULTIES COULD DELAY COMMERCIALIZATION OF OUR PRODUCTS.

Of the products that we currently have in clinical development, Roche is responsible for manufacturing Zenapax, SmithKline is responsible for manufacturing the humanized anti-IL-4 antibody and Scil Biomedicals is responsible for manufacturing the SMART Anti-L-Selectin Antibody. We are responsible for manufacturing our other products for our own development. We intend to continue to manufacture potential products for use in preclinical and clinical trials using our manufacturing facility in accordance with standard procedures that comply with appropriate regulatory standards. The manufacture of sufficient quantities of antibody products that comply with these standards is an expensive, time-consuming and complex process and is subject to a number of risks that could result in delays. We and our collaborative partners have experienced some manufacturing difficulties. Product supply interruptions could significantly delay clinical development of our potential products, reduce third party or clinical researcher interest and support of proposed clinical trials, and possibly delay commercialization and sales of these products. Manufacturing difficulties can even interrupt the supply of marketed products, thereby reducing revenues and risking loss of market share. For example, Roche has received a warning letter from the FDA regarding deficiencies in the manufacture of various products. Although the letter primarily related to products other than Zenapax, Roche has also experienced difficulties in the manufacture of Zenapax leading to interruptions in supply. If future manufacturing difficulties arise and are not corrected in a timely manner, Zenapax supplies could be interrupted, which could cause a delay or termination of our clinical trials of Zenapax in autoimmune disease and could force Roche to withdraw Zenapax from the market temporarily or permanently, resulting in loss of revenue to us. These occurrences could impair our competitive position.

We do not have experience in manufacturing commercial quantities of our potential products, nor do we currently have sufficient capacity to manufacture our potential products on a commercial scale. To obtain regulatory approvals and to create capacity to produce our products for commercial sale at an acceptable cost, we will need to improve and expand our existing manufacturing capabilities. We are reviewing plans to expand our manufacturing capacity, including possible acquisition and conversion of an existing building into a manufacturing plant or construction of an entirely new manufacturing plant. If we implement these plans we will incur substantial costs. Any construction delays could impair our ability to produce adequate supplies of our potential products for clinical use or commercial sale on a timely basis. Further, we may be unable to improve and expand our manufacturing capability sufficiently to obtain necessary regulatory approvals and to produce adequate commercial supplies of our potential products on a timely basis. Failure to do so could delay commercialization of these products and could impair our competitive position.

We are also investigating the use of contract manufacturing to produce commercial supplies of at least the SMART M195 Antibody in the event that the Phase III trial of that antibody is successful. We may be unable to secure such manufacturing capacity and to successfully produce commercial supplies on a timely basis. Failure to do so could delay commercialization of this product and could impair our competitive position.

WE MAY REQUIRE ADDITIONAL FUNDS THAT MAY BE DIFFICULT TO OBTAIN IN ORDER TO CONTINUE OUR BUSINESS ACTIVITIES AS PLANNED.

Our operations to date have consumed substantial amounts of cash. We will be required to spend substantial funds in conducting clinical trials, to expand our marketing capabilities and efforts, to expand existing research and development programs, to develop and expand our development and manufacturing capabilities and to defend or prosecute our patents and patent applications. To develop and commercialize our products we may need to raise substantial additional funds through equity or debt financings, collaborative arrangements, the use of sponsored research efforts or other means. Additional financing may not be available on acceptable terms, if at all, and may only be available on terms dilutive to existing stockholders or that would increase the amount of our indebtedness. Our inability to secure adequate funds on a timely basis could result in the delay or cancellation of programs that we might otherwise pursue.

OUR REVENUE MAY BE ADVERSELY AFFECTED BY COMPETITION AND RAPID TECHNOLOGICAL CHANGE.

Potential competitors have developed and are developing human and humanized antibodies or other compounds for treating autoimmune and inflammatory diseases, transplantation, asthma and cancers. In addition, a number of academic and commercial organizations are actively pursuing similar technologies, and several companies have developed or may develop technologies that may compete with our SMART antibody technology. Competitors may succeed in more rapidly developing and marketing technologies and products that are more effective than our products or that would render our products or technology obsolete or noncompetitive. Our collaborative partners may also independently develop products that are competitive with products that we have licensed to them. This could reduce our revenues under our agreements with these partners.

Any product that we or our collaborative partners succeed in developing and for which regulatory approval is obtained must then compete for market acceptance and market share. The relative speed with which we and our collaborative partners can develop products, complete the clinical testing and approval processes, and supply commercial quantities of the products to the market compared to competitive companies will affect market success. For example, Novartis, which has a significant marketing and sales force directed to the transplantation market, has received approval to market Simulect, a product competitive with Zenapax, in the U.S. and Europe. Since Novartis launched Simulect in the European Union earlier than Roche, Zenapax may have a smaller market share than Simulect and other available products.

RISKS RELATING TO OUR INDUSTRY

WE MAY BE UNABLE TO OBTAIN OR MAINTAIN REGULATORY APPROVAL FOR OUR PRODUCTS.

The manufacturing, testing and marketing of our products are subject to regulation by numerous governmental authorities in the U.S. and other countries. In the U.S., pharmaceutical products are subject to rigorous FDA regulation. Additionally, other federal, state and local regulations govern the manufacture, testing, clinical and nonclinical studies to assess safety and efficacy, approval, advertising and promotion of pharmaceutical products. The process of obtaining approval for a new pharmaceutical product or for additional therapeutic indications within this regulatory framework requires a number of years and the expenditure of substantial resources. Companies in the pharmaceutical and biotechnology industries, including us, have suffered significant setbacks in various stages of clinical trials, even in advanced clinical trials after promising results had been obtained in earlier trials.

In addition to the requirement for FDA approval of each pharmaceutical product, each pharmaceutical product manufacturing facility must be registered with, and approved by, the FDA. The manufacturing and quality control procedures must conform to rigorous guidelines in order to receive FDA approval. Pharmaceutical product manufacturing establishments are subject to inspections by the FDA and local authorities as well as inspections by authorities of other countries. To supply pharmaceutical products for use in the U.S., foreign manufacturing establishments must comply with these FDA approved

guidelines. These foreign manufacturing establishments are subject to periodic inspection by the FDA or by corresponding regulatory agencies in these countries under reciprocal agreements with the FDA. Moreover, pharmaceutical product manufacturing facilities may also be regulated by state, local and other authorities.

For the marketing of pharmaceutical products outside the U.S., we and our collaborative partners are subject to foreign regulatory requirements and, if the particular product is manufactured in the U.S., FDA and other U.S. export provisions. Requirements relating to the manufacturing, conduct of clinical trials, product licensing, promotion, pricing and reimbursement vary widely in different countries. Difficulties or unanticipated costs or price controls may be encountered by us or our licensees or marketing partners in our respective efforts to secure necessary governmental approvals. This could delay or prevent us, our licensees or our marketing partners from marketing potential pharmaceutical products.

Both before and after approval is obtained, a pharmaceutical product, its manufacturer and the holder of the Biologics License Application (BLA) for the pharmaceutical product are subject to comprehensive regulatory oversight. The FDA may deny a BLA if applicable regulatory criteria are not satisfied. Moreover, even if regulatory approval is granted, such approval may be subject to limitations on the indicated uses for which the pharmaceutical product may be marketed. Further, marketing approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems with the pharmaceutical product occur following approval. In addition, under a BLA, the manufacturer continues to be subject to facility inspection and the applicant must assume responsibility for compliance with applicable pharmaceutical product and establishment standards. Violations of regulatory requirements at any stage may result in various adverse consequences, which may include, among other adverse actions, withdrawal of the previously approved pharmaceutical product or marketing approvals and/or the imposition of criminal penalties against the manufacturer and/or BLA holder.

MANUFACTURING CHANGES MAY RESULT IN DELAYS IN OBTAINING REGULATORY APPROVAL OR MARKETING FOR OUR PRODUCTS.

Manufacturing of antibodies for use as therapeutics in compliance with regulatory requirements is complex, time-consuming and expensive. If we make changes in the manufacturing process, we may be required to demonstrate to the FDA and corresponding foreign authorities that the changes have not caused the resulting drug material to differ significantly from the drug material previously produced. This is particularly important if we want to rely on results of prior preclinical studies and clinical trials performed using the previously produced drug material. Depending upon the type and degree of differences between the newer and older drug material, we may be required to conduct additional animal studies or human clinical trials to demonstrate that the newly produced drug material is sufficiently similar to the previously produced drug material. We have made manufacturing changes and are likely to make additional manufacturing changes for the production of our products currently in clinical development. These manufacturing changes could result in delays in development or regulatory approvals or in reduction or interruption of commercial sales and could impair our competitive position.

OUR BUSINESS MAY BE HARMED IF WE CANNOT OBTAIN SUFFICIENT QUANTITIES OF RAW MATERIALS.

We depend on outside vendors for the supply of raw materials used to produce our product candidates. Once a supplier's materials have been selected for use in our manufacturing process, the supplier in effect becomes a sole or limited source of that raw material due to regulatory compliance procedures. If the third party suppliers were to cease production or otherwise fail to supply us with quality raw materials and we were unable to contract on acceptable terms for these services with alternative suppliers, our ability to produce our products and to conduct preclinical testing and clinical trials of product candidates would be adversely affected. This could impair our competitive position.

IF WE DO NOT ATTRACT AND RETAIN KEY EMPLOYEES, OUR BUSINESS COULD BE IMPAIRED.

To be successful we must retain our qualified clinical, manufacturing, scientific and management personnel. Because we are located in a high technology area, we face competition for personnel from other companies, academic institutions, government entities and other organizations. We are currently conducting a search for a chief financial officer, as well as other senior management personnel. If we are unsuccessful in filling these positions or retaining qualified personnel, our business could be impaired.

WE MAY BE SUBJECT TO PRODUCT LIABILITY CLAIMS, AND OUR INSURANCE COVERAGE MAY NOT BE ADEQUATE TO COVER THESE CLAIMS.

We face an inherent business risk of exposure to product liability claims in the event that the use of products during research and development efforts or after commercialization results in adverse effects. This risk will exist even with respect to any products that receive regulatory approval for commercial sale. While we have obtained liability insurance for our products, it may not be sufficient to satisfy any liability that may arise. Also, adequate insurance coverage may not be available in the future at acceptable cost, if at all.

WE MAY INCUR SIGNIFICANT COSTS IN ORDER TO COMPLY WITH ENVIRONMENTAL REGULATIONS OR TO DEFEND CLAIMS ARISING FROM ACCIDENTS INVOLVING THE USE OF HAZARDOUS MATERIALS.

We are subject to federal, state and local laws and regulations governing the use, discharge, handling and disposal of materials and wastes used in our operations. As a result, we may be required to incur significant costs to comply with these laws and regulations. We cannot eliminate the risk of accidental contamination or injury from these materials. In the event of such an accident, we could be held liable for any resulting damages and incur liabilities which exceed our resources. In addition, we cannot predict the extent of the adverse effect on our business or the financial and other costs that might result from any new government requirements arising out of future legislative, administrative or judicial actions.

CHANGES IN THE U.S. AND INTERNATIONAL HEALTH CARE INDUSTRY COULD ADVERSELY AFFECT OUR REVENUES.

The U.S. and international health care industry is subject to changing political, economic and regulatory influences that may significantly affect the purchasing practices and pricing of pharmaceuticals. Cost containment measures, whether instituted by health care providers or imposed by government health administration regulators or new regulations, could result in greater selectivity in the purchase of drugs. As a result, third-party payors may challenge the price and cost effectiveness of our products. In addition, in many major markets outside the U.S., pricing approval is required before sales can commence. As a result, significant uncertainty exists as to the reimbursement status of approved health care products.

We may not be able to obtain or maintain our desired price for our products. Our products may not be considered cost effective relative to alternative therapies. As a result, adequate third-party reimbursement may not be available to enable us to maintain prices sufficient to realize an appropriate return on our investment in product development. Also, the trend towards managed health care in the U.S. and the concurrent growth of organizations such as health maintenance organizations, as well as legislative proposals to reform health care or reduce government insurance programs, may all result in lower prices, reduced reimbursement levels and diminished markets for our products. These factors will also affect the products that are marketed by our collaborative partners.

RISKS RELATING TO THIS OFFERING

AS A RESULT OF OUR SALE OF CONVERTIBLE NOTES, WE HAVE A SIGNIFICANT AMOUNT OF DEBT AND MAY HAVE INSUFFICIENT CASH TO SATISFY OUR DEBT SERVICE OBLIGATIONS. IN ADDITION, THE AMOUNT OF OUR DEBT COULD IMPEDE OUR OPERATIONS AND FLEXIBILITY.

As a result of our sale of convertible notes with an aggregate principal amount of \$150 million in February 2000, we have a significant amount of debt and debt service obligations. If we are unable to generate sufficient cash flow or otherwise obtain funds necessary to make required payments on the notes, including from cash and cash equivalents on hand, we will be in default under the terms of the indenture which could, in turn, cause defaults under our other existing and future debt obligations. Our operations have not produced income sufficient to cover our fixed charges and we do not expect they will do so for at least the near future.

Even if we are able to meet our debt service obligations, the amount of debt we have could adversely affect us in a number of ways, including by:

- limiting our ability to obtain any necessary financing in the future for working capital, capital expenditures, debt service requirements or other purposes
- limiting our flexibility in planning for, or reacting to, changes in our business
- placing us at a competitive disadvantage relative to our competitors who have lower levels of debt
- making us more vulnerable to a downturn in our business or the economy generally, and
- requiring us to use a substantial portion of our cash to pay principal and interest on our debt, instead of applying those funds to other purposes such as working capital and capital expenditures.

OUR COMMON STOCK PRICE IS VOLATILE AND AN INVESTMENT IN OUR COMPANY COULD DECLINE IN VALUE.

Market prices for securities of biotechnology companies, including ourselves, have been highly volatile so that investment in our securities involves substantial risk. Additionally, the stock market from time to time has experienced significant price and volume fluctuations that may be unrelated to the operating performance of particular companies. The following are some of the factors that may have a significant effect on the market price of our common stock:

- developments or disputes as to patent or other proprietary rights
- disappointing sales of approved products
- approval or introduction of competing products and technologies
- results of clinical trials
- failures or unexpected delays in obtaining regulatory approvals or FDA advisory panel recommendations
- delays in manufacturing or clinical trial plans
- fluctuations in our operating results
- disputes or disagreements with collaborative partners
- market reaction to announcements by other biotechnology or pharmaceutical companies
- announcements of technological innovations or new commercial therapeutic products by us or our competitors
- initiation, termination or modification of agreements with our collaborative partners
- loss of key personnel

- litigation or the threat of litigation
- public concern as to the safety of drugs developed by us
- sales of our common stock held by collaborative partners or insiders
- comments and expectations of results made by securities analysts, and
- general market conditions.

If any of these factors causes us to fail to meet the expectations of securities analysts or investors, or if adverse conditions prevail or are perceived to prevail with respect to our business, the price of the common stock would likely drop significantly. A significant drop in the price of a company's common stock often leads to the filing of securities class action litigation against the company. This type of litigation against us could result in substantial costs and a diversion of management's attention and resources.

USE OF PROCEEDS

We estimate the net proceeds to us from the sale of the common stock offered hereby will be approximately \$355.6 million (or \$409.0 million if the over-allotment option is exercised in full) after deducting underwriting discounts and commissions and the estimated offering expenses payable by us. We expect to use the net proceeds to fund clinical trials, to expand manufacturing capabilities, to expand marketing and sales capabilities, and for working capital and other general corporate purposes. Pending use of the net proceeds of this offering, we intend to invest the net proceeds in interest-bearing, investment-grade securities.

PRICE RANGE OF COMMON STOCK

Our common stock trades on The Nasdaq National Market under the symbol "PDLI." The following table sets forth for the periods indicated the high and low closing bid prices for our common stock as quoted on The Nasdaq National Market

| | HIGH | | LOW | |
|--|--------------------|--------------------------|---------|-------------------------|
| 1998 First QuarterSecond QuarterThird QuarterFourth Quarter | 19 13 | 1/8 3/4 1/8 5/8 | 10 8 | 1/16 |
| 1999 First QuarterSecond QuarterThird QuarterThird QuarterFourth Quarter. | 11 18 | 1/4 1/16 5/16 | 7 11 | 3/16 1/16 |
| 2000 First QuarterSecond QuarterThird Quarter (through September 22, 2000) | \$163 92 124 | 5/8 | 29 | 49/64 25/32 19/32 |

On September 22, 2000, the closing bid price quoted on The Nasdaq National Market for the common stock was \$124 per share. As of September 22, 2000 there were approximately 126 holders of record of our common stock. Because many of these shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings for use in the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Payment of future dividends, if any, will be at the discretion of our board of directors after taking into account various factors, including our financial condition, operating results and current and anticipated cash needs.

CAPITALIZATION

The following table presents our actual unaudited capitalization as of June 30, 2000 and our adjusted capitalization reflecting the estimated net proceeds of \$355.6 million from the sale of the 3,000,000 shares of common stock offered in this offering. This table should be read with the financial statements and related notes incorporated by reference into this prospectus.

| | JUNE 3 | 30, 2000 |
|---|----------------------------|------------------------|
| | ACTUAL | AS ADJUSTED |
| | (IN TH | DUSANDS) |
| Long-term debt, excluding current maturities | • | \$ 9,527 150,000 |
| Stockholders' equity: Preferred stock, par value \$0.01 per share, 10,000,000 shares authorized; no shares issued and outstanding Common stock, par value \$0.01 per share, 90,000,000 shares authorized; 39,849,124 issued and outstanding actual, 42,849,124 shares outstanding as adjusted Additional paid-in capital | 398 260,919 (73,426) | (73, 426) |
| Accumulated other comprehensive income (loss) Total stockholders' equity | (2,221) 185,670 | (2,221) 541,278 |
| Total capitalization | \$345,197 ====== | |

This table excludes (a) options outstanding under our stock option plans at June 30, 2000 to purchase 5,227,090 shares of common stock at a weighted average exercise price of \$21.98, of which options to purchase 1,463,383 shares were then exercisable, (b) 730,608 shares authorized for issuance under our employee stock purchase plan, and (c) 1,986,755 shares issuable upon conversion of our convertible notes.

DILUTION

The net tangible book value of our common stock as of June 30, 2000 was \$180,887,600 or \$4.54 per share. Net tangible book value per share represents the amount of our total tangible assets less our total liabilities divided by the number of shares of common stock outstanding. After giving effect to the sale of 3,000,000 shares of common stock, less underwriting discounts and commissions and our estimated offering expenses, our pro forma net tangible book value as of June 30, 2000 would have been \$536,495,100, or \$12.52 per share. This represents an immediate increase in pro forma net tangible book value of \$7.98 per share to existing investors and an immediate dilution per share of \$112.43 to new investors purchasing shares of common stock in this offering. Dilution per share to new investors represents the difference between the price per share of common stock in this offering and the pro forma net tangible book value per share immediately afterwards.

| Assumed public offering price per share | | \$124.95 |
|--|--------|----------|
| Net tangible book value per share as of June 30, 2000 | \$4.54 | |
| Increase per share attributable to new investors | 7.98 | |
| | | |
| Pro forma net tangible book value per share after this | | |
| offering | | 12.52 |
| | | |
| Dilution per share to new investors | | \$112.43 |
| | | ====== |

If the underwriters' over-allotment option is exercised in full, the pro forma net tangible book value per share will be \$13.62, resulting in immediate dilution to new investors of \$111.33 per share.

This table excludes all options and warrants that will remain outstanding upon completion of this offering. At June 30, 2000, a total of 5,227,090 shares of common stock were subject to outstanding options, at a weighted average exercise price of \$21.98 per share. The exercise of outstanding options and warrants having an exercise price less than the offering price would increase the dilutive effect to new investors.

SELECTED FINANCIAL DATA

The following selected financial data for each of the three years in the period ended December 31, 1999, and as of December 31, 1998 and 1999 has been taken from, or is derived from, and should be read with our financial statements, including the notes thereto, that have been audited by ${\sf Ernst}\ \&\ {\sf Young}$ LLP, independent auditors, and are incorporated by reference herein and included in our Annual Report on Form 10-K for the year ended December 31, 1999. The selected financial data for each of the years ended December 31, 1995 and 1996, and as of December 31, 1995, 1996 and 1997, has been taken from or is derived from our audited financial statements that have not been included or incorporated by reference in this prospectus. The selected financial data for the six-month periods ended June 30, 1999 and 2000, and as of June 30, 2000 is unaudited and has been taken from or is derived from, and should be read with our unaudited financial statements incorporated by reference herein and included in our Quarterly Report on Form 10-Q for the quarter ended June 30, 2000. The unaudited financial statements have been prepared on the same basis as the audited financial statements and include all adjustments, consisting only of normal, recurring adjustments, that in the opinion of management are necessary for a fair presentation of the information set forth therein. Historical results are not necessarily indicative of future results for any period.

This financial data is qualified by reference to, and should be read in conjunction with, the financial statements incorporated by reference into this prospectus.

| | | YEAR ENDED DECEMBER 31, | | | | SIX MONTH JUNE | |
|--|---------------------|-------------------------|----------------------|---------------------|----------------------|---------------------|--------------------|
| | 1995 | 1996 | 1997 | | 1999 | 1999 | 2000 |
| | | (IN | THOUSANDS, | EXCEPT PER | SHARE DATA | ·) | |
| STATEMENTS OF OPERATIONS DATA: | | | | | | | |
| Revenues: | | | | | | | |
| Revenue under agreements with third parties Interest and other | \$11,408 | \$ 16,500 | \$ 11,137 | \$21,325 | \$ 26,811 | \$12,501 | \$28,343 |
| income | 6,205 | 6,100 | 9,118 | 9,503 | 8,943 | 4,623 | 7,521 |
| Total revenues Costs and expenses: | 17,613 | 22,600 | 20,255 | | 35,754 | 17,124 | 35,864 |
| Research and development General and | 20,803 | 28,795 | 25,614 | 31,645 | 36,090 | 16,793 | 21,284 |
| administrative | | 5,601 | | , | 9,842 | 4,895 | 5,329 |
| Special charge | | | 11,887 | | | | |
| Interest expense | 1 | | | | 155 | | 3,460 |
| Total costs and expenses | | | 44,130 | 40,330 | 46,087 | 21,688 | 30,073 |
| Net income (loss) | \$(8,354) ===== | \$(11,796) ====== | \$(23,875) ====== | \$(9,502) ====== | \$(10,333) ====== | \$(4,564) ===== | \$ 5,791 ====== |
| Net income (loss) per share | | | | | | | |
| Basic | \$ (0.27) ====== | \$ (0.38) ====== | \$ (0.68) ====== | \$ (0.26) ====== | \$ (0.28) ====== | \$ (0.12) ====== | \$ 0.15 ====== |
| Diluted | \$ (0.27) ====== | \$ (0.38) ====== | \$ (0.68) ====== | \$ (0.26) ====== | \$ (0.28) ====== | \$ (0.12) ====== | \$ 0.13 ====== |
| Shares used in computation of net income (loss) per share | | | | | | | |
| Basic Diluted | | | | | 37,396 37,396 | | 39,218 43,186 |
| 522000011111111111111111111111111111111 | 55,555 | 01,200 | 55,250 | 0.,000 | 0.,000 | 31,244 | -0, 100 |

| | DECEMBER 31, | | | | | JUNE 30, |
|---|--|--|--|--|--|---|
| | 1995 | 1996 | 1997 | 1998 | 1999 | 2000 |
| | | | | | | |
| BALANCE SHEET DATA: Cash, cash equivalents and investments | \$107,065 43,522 116,412 (23,711) | \$ 99,667 74,221 110,331 (35,507) | \$163,655 66,490 175,026 (59,382) | \$143,439 82,394 171,850 (68,884) | \$137,237 22,669 182,551 (79,217) | \$309,881 194,468 354,658 (73,426) |
| Long-term obligations, exclusive of current portion Total stockholders' equity | 112,856 | 105,112 | 168,468 | 162,496 | 9,724 164,743 | 159,527 185,670 |

The non-cash special charge of approximately \$11.9 million in 1997 related to the extensions of the term of all outstanding stock options held by our employees, officers, directors and consultants that were granted prior to February 1995, with the single exception of stock options granted to one non-employee director. The extension conforms the term of previously granted stock options, which was six years, to those granted since February 1995, ten years.

BUSINESS

OVERVIEW

We are a leader in the development of humanized monoclonal antibodies for the prevention and treatment of disease. We have licensed rights to our first humanized antibody product, Zenapax, to Roche, which markets it for the prevention of kidney transplant rejection. We are also testing Zenapax for the treatment of autoimmune disease. In addition, we have eight other humanized antibodies in clinical development for autoimmune and inflammatory conditions, asthma and cancer.

We have fundamental patents in the U.S., Europe and Japan, which we believe cover most humanized antibodies. Eleven companies have licenses under these patents for humanized antibodies that they have developed. We receive royalties on sales of the three humanized antibodies developed by other companies that are currently being marketed.

PRODUCTS IN DEVELOPMENT

The following table summarizes the potential therapeutic applications and development status for our approved product and clinical product candidates. Not all clinical trials being conducted are listed. The development and commercialization of our product candidates is subject to numerous risks and uncertainties.

| ANTIBODY PRODUCT | INDICATION(S) | STATUS |
|-----------------------------|------------------------------|--|
| | | |
| Zenapax | Kidney transplant rejection | Marketed |
| | Heart transplant rejection | Phase III |
| | Psoriasis | Phase II |
| | Uveitis | Phase I/II |
| | Multiple sclerosis | Phase I/II |
| SMART M195 | Acute myeloid leukemia | Phase III |
| Nuvion | Psoriasis | Phase I/II |
| | Transplantation | Phase II |
| | Graft-versus-host disease | Phase I |
| | Cutaneous T-cell lymphoma | Phase I |
| SMART Anti-L-Selectin | Trauma | Phase IIa |
| SMART 1D10 | Non-Hodgkins B-cell lymphoma | Phase I |
| Humanized Anti-IL-4 | Asthma | Phase I |
| SMART Anti-Gamma Interferon | Autoimmune diseases | Phase I |
| SMART Anti-VEGF | Cancer | Phase I |
| SMART Anti-E/P-Selectin | Stroke, asthma | Phase I in healthy volunteers complete |

ZENAPAX. The FDA approved Zenapax in December 1997 for the prevention of kidney transplant rejection. It has since been approved in Europe and other countries. Zenapax was the first humanized antibody to be approved anywhere in the world. The Zenapax approvals are based on two Phase III clinical trials, both of which demonstrated that Zenapax-treated patients had a statistically significant reduction in acute rejection episodes compared to patients who did not receive Zenapax. Also, Zenapax treatment was not associated with any observed side effects in addition to those typically seen in the transplant setting. Our licensee Roche sells Zenapax in the U.S., Europe and other territories for the transplant indication and we receive royalties on Zenapax sales

Roche has sponsored or authorized several additional Zenapax clinical trials in other transplant settings, including liver transplants, pediatric kidney transplants, in combination with Roche's drug CellCept with and without certain other immunosuppressive drugs in kidney transplants, and for the treatment of graft-versus-host disease in donor bone marrow transplants. Roche is currently conducting a Phase III trial in heart transplant

patients. In addition, we are aware of numerous independent clinical studies using Zenapax in settings including heart, lung, pancreas and combined intestinal and liver transplants.

Zenapax binds to the interleukin-2 (IL-2) receptor on immune system cells known as T cells. IL-2 is a lymphokine, one of the substances released by cells as part of the immune response that occurs in autoimmune diseases and often following organ transplants. IL-2 stimulates T cells to divide and participate in an immune response. Zenapax blocks the binding of IL-2 to its receptor on T cells, suppressing an immune response by inhibiting the proliferation of activated T cells.

Zenapax is the first effective immunosuppressive drug without significant side effects. For example, Zenapax is more specific and less toxic than other immunosuppressive drugs such as cyclosporine or ORTHOCLONE OKT3 which suppress essentially all T cells and possibly other cells. As a result, we believe Zenapax may be useful for the long-term treatment of autoimmune diseases such as psoriasis and multiple sclerosis.

In 1999, we reacquired from Roche specific development and marketing rights to Zenapax for autoimmune diseases. We will fund costs of clinical trials for Zenapax in autoimmune diseases. In return, we have the right to market Zenapax for approved autoimmune indications in the U.S. and Canada, and will receive a major portion of the revenues from sales for these diseases. Roche will continue to manufacture Zenapax and pay for the cost of goods from its share of the revenues. In Europe and other countries, Roche can elect to market Zenapax for approved autoimmune indications or to allow us to market it, and revenues will be shared.

Zenapax is currently in two Phase II trials in psoriasis, a common autoimmune disease of the skin, and in early stage trials for uveitis, multiple sclerosis, aplastic anemia, and the ocular manifestations of Bechet's disease. We plan to conduct additional trials for psoriasis and other autoimmune diseases. In the early stage clinical trial for uveitis, an autoimmune disease of the eye, Zenapax was safely administered to patients for one year and was effective in controlling the disease in most patients, some of whom have continued to receive Zenapax for up to three years.

SMART M195 ANTIBODY. SMART M195 binds to the cancer cells of most patients with myeloid leukemias. Myeloid leukemia is the major form of adult leukemia. It is classified into two types: acute myeloid leukemia, or AML, and chronic myelogenous leukemia. At least 14,000 new cases of myeloid leukemia occur each year in the U.S. and 10,000 or more of these cases are AML. The current survival rate from myeloid leukemia is very low, despite aggressive chemotherapy and multiple, expensive hospitalizations.

Several clinical trials using the SMART M195 Antibody have been conducted, including:

- a multicenter Phase II/III trial designed to evaluate the antibody for prolonging remission in AML patients
- a Phase II trial to evaluate whether the antibody could induce remission in patients whose AML had relapsed
- a physician-sponsored Phase II trial of the antibody in patients with newly diagnosed acute promyelocytic leukemia, a subtype of AML, and
- physician-sponsored trials using the antibody linked to the radioisotopes 90-Yttrium or 213-Bismuth.

In general, these trials have demonstrated that SMART M195 has some biological activity and potential for efficacy. In November 1999, we began a randomized, multicenter, international Phase III study of the antibody in patients with refractory or first-relapsed AML. Patients receive a regimen of either SMART M195 plus standard chemotherapy or standard chemotherapy alone. Up to 200 patients may be enrolled in the trial, which is designed to evaluate the frequency of complete remission and other endpoints. An interim review of the trial results by an independent data safety monitoring board is expected in the fourth quarter of 2000. The monitoring board could recommend or require that the trial be

terminated if the interim data do not show a sufficient probability of the trial being successful or if specified safety criteria are not met. If the final results of the trial are positive, we expect to file for marketing approval.

In addition to the Phase III trial, in 1999 a Phase II trial began to test the safety and efficacy of SMART M195 in patients with high risk myelodysplastic syndrome, a precancerous condition. The study is being conducted by the European Organization for the Research and Treatment of Cancer.

NUVION (SMART ANTI-CD3 ANTIBODY). We are developing this antibody for the treatment of autoimmune diseases. It binds to the CD3 antigen, a key receptor for stimulating T cells. A mouse anti-CD3 antibody, ORTHOCLONE OKT3, from Johnson & Johnson, is marketed as an immunosuppressive drug for the treatment of acute kidney, liver and heart transplantation rejection. While highly effective, OKT3 use is often limited by serious toxicity as well as formation of anti-OKT3 antibodies because it is a mouse antibody. In contrast, Nuvion is humanized and also has been specifically engineered to reduce certain immune system interactions that we believe contribute to the toxicity of OKT3.

Although both Nuvion and Zenapax may target some of the same diseases, we believe they may have complementary roles in medical treatment. Nuvion may be more potent than Zenapax, but may not be suitable for chronic administration, so it may be most useful to treat acute episodes of autoimmune disease and to induce remissions. Zenapax may be useful to maintain the remissions for longer periods.

Nuvion is currently in a Phase I/II clinical trial for psoriasis. It is also in clinical trials for transplant rejection, graft-versus-host disease, and cutaneous T-cell lymphoma, but we have no current plans to conduct Phase III trials in these indications. We have retained worldwide rights to Nuvion.

SMART ANTI-L-SELECTIN ANTIBODY. This antibody inhibits the process of neutrophil binding to the lining of blood vessels. It may be useful for preventing multiple organ failure and mortality that often follows severe trauma. In primate studies carried out by independent investigators, SMART Anti-L-Selectin treatment resulted in a statistically significant improvement in survival in a model that simulates severe trauma. We believe this antibody also may be useful to treat adult respiratory distress syndrome and reperfusion injury due to heart attacks.

In May 1999, we licensed European marketing rights for this antibody to Scil, a European biotechnology company. Scil paid us a licensing fee and agreed to conduct and pay for clinical trials in Europe and to provide us with the data; in return, we are making milestone payments to Scil, at our election, on the achievement of defined clinical and regulatory goals. Scil has completed a Phase I trial of SMART Anti-L-Selectin and is now conducting a Phase IIa trial for treatment of trauma. If the results from that Phase IIa trial are encouraging, we may initiate clinical development in the U.S.

SMART 1D10 ANTIBODY. The National Cancer Institute is sponsoring a Phase I trial of this antibody for non-Hodgkins B-cell lymphoma. Clinical responses were observed in three of the patients in this trial, and we plan to initiate a Phase II trial. SMART 1D10 is directed to a different target on B cells than Rituxan, the antibody currently marketed for non-Hodgkins lymphoma, and thus may provide an alternative therapy. In the U.S., approximately 290,000 patients have this disease and 55,000 new cases occur annually. We have retained worldwide rights to SMART 1D10.

HUMANIZED ANTI-IL-4 ANTIBODY. We licensed this antibody, for the potential treatment of asthma and allergy, from SmithKline in 1999. The humanized anti-IL-4 antibody blocks the effects of interleukin 4, which is believed to play a key role in initiating the series of biological processes that lead to allergy and asthma. SmithKline began a Phase I trial of the humanized anti-IL-4 antibody, which we have now completed. We plan to initiate a Phase I/II multiple dose study, followed by a Phase II trial in moderate to severe asthma patients.

We will conduct and pay for initial clinical trials of the humanized anti-IL-4 antibody and pay SmithKline to manufacture the antibody. SmithKline has agreed to make a milestone payment to us upon the achievement of a specified clinical goal. At the completion of a specified Phase II trial, SmithKline may choose to pay us a fee to acquire marketing rights. In that case, we and SmithKline will share future

development costs and profits from any product sales. If SmithKline elects not to pay this fee, we will have the right to develop and market the antibody.

Concurrently, we granted SmithKline an exclusive license under our humanization patents for a humanized anti-IL-5 antibody that they are developing, for which SmithKline paid us a licensing fee. We also granted SmithKline options to obtain non-exclusive licenses under these patents for up to three additional antibodies. These arrangements with SmithKline illustrate our ability to leverage our patent portfolio to obtain rights to a potentially important product.

SMART ANTI-GAMMA INTERFERON ANTIBODY. This antibody targets gamma interferon, a protein that stimulates several types of white blood cells and that may be involved in some autoimmune diseases. We have completed a Phase I trial of SMART Anti-Gamma Interferon in normal volunteers, which showed the antibody is well-tolerated and has biological activity. We plan to initiate a Phase I/II trial in patients with Crohn's disease, a form of inflammatory bowel disease. In the future, we may initiate clinical trials in other autoimmune diseases. We have retained worldwide rights to SMART Anti-Gamma Interferon.

SMART ANTI-VEGF ANTIBODY. This antibody blocks the action of vascular endothelial growth factor (VEGF), which is believed to play an important role in the formation of blood vessels in tumors, a process that allows the tumors to grow. We humanized the antibody for Toagosei, a Japanese chemical company, and subsequently entered into an agreement with Toagosei under which the two companies will share development costs, marketing rights, and profits from potential sales of the antibody in markets outside of Japan. Toagosei has exclusive rights to market the antibody in Japan. We have exclusive marketing rights in North America and the option to obtain marketing rights in the rest of the world outside of Japan. We are conducting a Phase I trial of the antibody in Callaboration with the European Organization for Research and Treatment of Cancer.

SMART ANTI-E/P-SELECTIN ANTIBODY. This antibody targets adhesion molecules on the inside of blood vessels that may be involved in inflammation. We have completed a Phase I trial of SMART Anti-E/P-Selectin in healthy volunteers which showed that the antibody is well-tolerated in a range of doses. We have retained worldwide rights to SMART Anti-E/P-Selectin and are seeking a partner for its further development.

OUR TECHNOLOGIES

Antibody Background Information

Antibodies are protective proteins released by the immune system's B cells, a type of white blood cell, in response to the presence of a foreign substance in the body, such as a virus, or due to an aberrant autoimmune response. B cells produce millions of different kinds of antibodies, which have slightly different shapes that enable them to bind and, as a result, inactivate different targets. Antibodies that have identical molecular structure that bind to a specific target are called monoclonal antibodies.

Typically, mice have been used to produce monoclonal antibodies to a wide range of targets, including targets to which the human body does not normally produce antibodies. Specifically, many mouse, or murine, antibodies have been developed as potential therapeutics to inhibit immune function, destroy cancer cells or neutralize viruses.

Although murine monoclonal antibodies are relatively easy to generate, they have significant drawbacks as therapeutics. Murine antibodies have a relatively short half-life in human patients, requiring them to be administered frequently. In addition, murine antibodies are not adapted to work effectively with the human immune system and therefore often have limited ability to destroy the target, such as cancer cells. Most importantly, when injected into humans, a murine antibody is usually recognized by the body's immune system as foreign. The immune system therefore responds with a human anti-mouse antibody, or HAMA, response, which rapidly neutralizes the murine antibody and renders it ineffective for further therapy. These problems have largely prevented murine antibodies from fulfilling their promise as therapeutics.

More recently, improved forms of antibodies, such as humanized, human and chimeric antibodies, have been developed using recombinant DNA and other technologies. These new antibodies can minimize or avoid many of the problems associated with murine antibodies and have led to a resurgence of interest in antibody therapeutics by the pharmaceutical and biotechnology industries. As a result of these advances, many monoclonal antibodies are now progressing into clinical trials. In a list of biotechnology medicines under clinical development in the U.S. published in 1999 by the Pharmaceutical Research and Manufacturers of America, antibodies comprised the single largest category (excluding vaccines), representing 22% of the products listed. In particular, we are aware of at least 40 humanized antibodies in clinical trials, including several antibodies addressing large markets that are being developed by major pharmaceutical companies. Eight humanized or chimeric antibodies have already been approved for marketing by the FDA, and generated more than \$1.0 billion in revenues in 1999.

Our SMART Antibody Technology

Our patented SMART antibody technology has positioned us as a leader in the development of therapeutic antibodies that overcome the problems associated with murine antibodies. Our SMART antibodies are human-like antibodies designed using structural information from promising murine antibodies to capture the benefits of such antibodies while overcoming many of their limitations in treating humans. Clinical trials and preclinical studies have shown that our SMART antibodies generally avoid a HAMA response and have a longer half-life than murine antibodies.

Every antibody contains two regions: a variable domain that binds to the target antigen and a constant domain that interacts with other portions of the immune system. The variable domain is composed of the complementarity determining regions (CDRs) that directly bind to the target antigen and the framework region that holds the CDRs in position and helps maintain their required shape. Researchers have used genetic engineering to construct humanized antibodies that consist of the CDRs from a murine antibody with the framework region and constant domain from a human antibody. However, when the CDRs from the murine antibody are combined with the framework of the human antibody, the human framework often distorts the shape of the CDRs so they no longer bind well to the target. Therefore, it is usually necessary to substitute one or more amino acids from the murine antibody into the framework of the humanized antibody for it to maintain the binding ability of the murine antibody.

A SMART antibody is a humanized antibody designed by using our proprietary computer technology to guide the choice of substitutions of amino acids from the murine antibody into the human antibody framework, based on structural information derived from the murine antibody. The construction of a SMART antibody starts with the identification of a murine antibody that has demonstrated favorable results in laboratory, animal or human studies. A model of the murine antibody is generated using proprietary computer modeling software that predicts the shapes of antibodies and eliminates the need for more time-consuming laboratory techniques. The resulting model is carefully analyzed to identify the few key amino acids in the framework most responsible for maintaining the shape of the CDRs. Software we developed as well as the experience of our computational chemists is important in this analysis. These few key murine amino acids are substituted into the human framework of the SMART antibody along with the murine CDRs in order to maintain their ability to bind well to the target. The resulting SMART antibody retains most or all of the binding ability of the murine antibody, but is about 90% human.

Our Other Technologies

In addition to our SMART antibody technology, we use additional antibody-based drug development technologies to overcome shortcomings of murine antibodies. We are also pursuing a program to discover novel antibiotics and a rational drug design program that leverages our computer expertise to potentially develop new drug candidates.

NOVEL ANTIBIOTICS. We have a research program to discover and develop new antibiotics for the treatment of certain microbial infections, including infections caused by microbes that have developed resistance to available antibiotics. This program uses technology to identify microbial genes that are

differentially expressed when microbes infect a host. These microbial genes and their products may become potential targets for novel antibiotics, which may be identified by high throughput screening and medicinal chemistry. We anticipate that aspects of this work may be conducted by corporate partners. In December 1997, we entered into a collaborative agreement with Eli Lilly and Company, providing for a funded research program involving seven specific types of bacteria. The funded research program will end on November 30, 2000.

RATIONAL DRUG DESIGN. We are pursuing a rational drug design program focusing on small molecules by extending our computer modeling tools originally developed for our SMART antibody program. Rational drug design uses computer models of proteins and their interactions with smaller molecules to accelerate discovery and optimization of new drug compounds. Although our technology is at an early stage, we believe that this application of our modeling algorithms may ultimately be used to develop non-antibody, small-molecule drug candidates. For that purpose, we have initiated a program in medicinal and combinatorial chemistry.

BUSINESS STRATEGY

Our objective is to leverage our product pipeline and patent portfolio in the field of antibodies to become a fully-integrated, profitable, research-based biopharmaceutical company. We derive revenues, and expect to derive revenues in the future, from three major sources:

- SALES OF PRODUCTS THAT WE HAVE DEVELOPED. We receive royalties on sales of Zenapax by our licensee, Roche. We have eight other humanized antibodies in clinical development. We plan to market some of our products, once approved, in North America, especially for specialty markets such as cancer that we believe can be effectively serviced with a relatively small sales force. We may license marketing rights for some antibodies or some geographic areas to other pharmaceutical companies.
- ROYALTIES FROM THE SALE OF HUMANIZED ANTIBODIES DEVELOPED BY OTHER COMPANIES. We license our patents covering humanized antibodies in return for license fees, annual maintenance payments and royalties on product sales. The three humanized antibodies currently approved by the FDA in addition to Zenapax are licensed under our patents. Two of these antibodies are Genentech's Herceptin and MedImmune's Synagis, which had reported sales totaling approximately \$480 million in 1999 and on which we are currently receiving royalties. The third is American Home Products' Mylotarg, which it began marketing in May 2000. We have license agreements with eight other companies for humanized antibodies they are developing.
- RESEARCH AND DEVELOPMENT CONTRACTS WITH OTHER COMPANIES. We humanize antibodies for other companies in return for upfront fees, milestone payments and royalties on any product sales. In some cases we also receive the right to co-promote these products in designated territories. We also sometimes license out marketing rights to a humanized antibody that we are developing, and then typically receive upfront fees and milestone payments and/or research funding, in addition to royalties on any product sales by our licensee.

COLLABORATIVE, HUMANIZATION AND PATENT LICENSING ARRANGEMENTS

Collaborative Arrangements

ROCHE. In 1989, we entered into agreements with Roche to collaborate on the research and development of antibodies which bind to the IL-2 receptor, including Zenapax. Under these agreements, Roche has exclusive, worldwide rights to manufacture, market and sell Zenapax. We began receiving royalties on sales of Zenapax in 1998. Our royalties are subject to offsets for milestones, third party license fees and royalties, and patent expenses paid by Roche.

In October 1999, we agreed with Roche to replace the 1989 agreements with new agreements under which we assumed worldwide responsibility for the clinical development of Zenapax for the potential

treatment of autoimmune diseases. Roche retained exclusive worldwide rights to Zenapax for non-autoimmune diseases and is continuing to market Zenapax for the prevention of kidney transplant rejection. In return for undertaking clinical development in autoimmune indications, we will receive a significant share of Zenapax revenues from sales for autoimmune indications, either from our own marketing efforts or from revenue sharing with Roche.

In the U.S. and Canada, we will have the right to market Zenapax in autoimmune indications and will pay for these activities from our share of revenues. Outside the U.S. and Canada, Roche may choose to market Zenapax in autoimmune indications. In this case, we will receive a substantial portion of Zenapax revenue from these indications. For countries and indications for which Roche elects not to market, we will receive an exclusive license to market Zenapax and pay Roche a small royalty.

SCIL. In March 1999, we entered into an agreement with Scil for rights to develop and market SMART Anti-L-Selectin in Europe. Scil paid us a \$3.0 million signing and licensing fee for these rights, and we will be entitled to royalties on any product sales. We agreed to make milestone payments to Scil, at our election, upon the achievement of specified clinical and regulatory goals.

SMITHKLINE. In September 1999, we signed agreements with SmithKline involving two humanized antibodies for the possible treatment of asthma. We obtained a license to SmithKline's humanized anti-IL-4 antibody and granted an exclusive license under our antibody humanization patents to SmithKline for its humanized anti-IL-5 antibody. We have completed the Phase I clinical program for the humanized anti-IL-4 antibody and plan to conduct Phase I/II and Phase II trials in asthma patients. We will be entitled to exclusive, worldwide development, marketing and sales rights to the anti-IL-4 antibody unless SmithKline pays a fee to acquire marketing rights at the end of a specified Phase II trial. If SmithKline decides to participate in the further development of the antibody, we will share future development costs and profits at a pre-agreed ratio. We also may receive co-promotion rights in the U.S.

TOAGOSEI. In July 1999, we signed a licensing and joint development agreement with Toagosei for an antibody developed by Toagosei and humanized by us. The antibody, SMART Anti-VEGF, binds to vascular endothelial growth factor, a protein that regulates new blood vessel formation in certain tissues and in tumors. We plan to develop the antibody with Toagosei for potential uses in the treatment of cancer.

Under the agreement, we obtained exclusive development and marketing rights to SMART Anti-VEGF in North America and the option to obtain exclusive rights to market the antibody in Europe and other markets, except Japan. Toagosei has exclusive rights to market SMART Anti-VEGF in Japan. We will direct the clinical development program, and the two companies will share development costs and profits from sales of the antibody, if any, in markets outside Japan.

LILLY. In December 1997, we signed a collaborative agreement with Lilly to discover and develop new small molecule drugs for the treatment of some types of infections, including those caused by organisms that are resistant to available antibiotics. The agreement involves a program to identify microbial genes that are differentially expressed when an infectious agent, such as a bacteria, infects a host. Lilly recently informed us that it does not intend to renew the research program under this agreement beyond the initial three-year term, which will end on November 30, 2000.

We received an initial \$3.0 million payment under the agreement and have received research funding totaling \$4.8 million over the three-year term. We also may receive milestone payments for identification of gene targets and for each compound selected for development by Lilly, if any, and are entitled to royalties on any product sales.

Humanization and Patent Licensing Arrangements.

YAMANOUCHI PHARMACEUTICAL CO., LTD. In February 1991, we entered into an agreement with Yamanouchi to humanize a mouse anti-platelet (anti-gpIIb/IIIa) antibody developed by Yamanouchi for cardiovascular disorders. Yamanouchi is conducting a Phase II clinical trial with the antibody we humanized for them. Yamanouchi has exclusive, worldwide rights to the antibody and is responsible for all

development activities. We have received milestone payments and will be entitled to royalties on any sales of the antibody.

MOCHIDA PHARMACEUTICAL CO., LTD. In December 1995, we entered into an agreement with Mochida to humanize a mouse antibody for use in infectious disease. We received a licensing and signing fee and milestone payments and can earn royalties on any product sales. In addition, we have an option to copromote the antibody in North America.

TOAGOSEI CO., LTD. In September 1996, we entered into an agreement with Toagosei to humanize a mouse antibody for treating cancer. We received a licensing and signing fee and milestone payments and can earn royalties on any product sales. In 1997, Toagosei made a \$2.0 million private equity investment in our company.

GENETICS INSTITUTE, INC. In December 1996, we entered into an agreement with Genetics Institute, now a wholly-owned subsidiary of American Home Products, to initially humanize three mouse antibodies that regulate an immune system pathway. To date, we have received a \$2.5 million licensing and signing fee and three milestone payments. We are entitled to royalties on any product sales. We also received an option to co-promote the products in North America under certain conditions.

TEIJIN LIMITED. In March 1997, we entered into an agreement with Teijin to humanize a mouse antibody to a toxin produced by the E. coli 0157 bacteria that can cause serious illness or death from the consumption of contaminated food. We have received a licensing and signing fee and milestone payment and are entitled to royalties on any product sales.

AJINOMOTO CO., INC. In July 1997, we entered into an agreement with Ajinomoto to humanize a mouse antibody directed at cardiovascular conditions. We have received a licensing and signing fee and milestone payments and are entitled to royalties on any product sales. In addition, we received the right to obtain co-promotion rights to the antibody in North America.

GENENTECH, INC. In September 1998, we entered into an agreement covering patent rights under our humanization patents and under Genentech patents relating to antibody engineering. Genentech paid us a \$6.0 million fee, and we paid Genentech a \$1.0 million fee. Each company can obtain up to six licenses for humanized antibodies upon payment of an additional fee of at least \$1.0 million per antibody, as well as royalties on any product sales. The number of licensed antibodies may be increased and the term of the agreement extended upon payment of additional fees. In November 1998, Genentech exercised certain of its rights under the agreement and obtained a nonexclusive license for Herceptin. Genentech paid us a \$1.0 million licensing and signing fee and we currently receive royalties on Herceptin sales.

PROGENICS PHARMACEUTICALS, INC. In April 1999, we entered into an agreement to humanize PRO 140, Progenic's novel anti-CCR5 monoclonal antibody that inhibits HIV replication in the laboratory. Progenics paid us a licensing and signing fee and has agreed to make additional payments upon the achievement of specified milestones and to pay royalties on any sales of the antibody.

FUJISAWA PHARMACEUTICALS CO. In June 1999, we entered into a research agreement with Fujisawa to engineer certain antibodies targeted to the treatment of inflammatory and immunologically-based disorders. The engineering included the use of our patented modification of the constant region of certain types of antibodies. In February 2000, we entered into an agreement to humanize one of these antibodies. Fujisawa paid us a \$1.5 million licensing and signing fee. We are entitled to receive milestone payments, annual maintenance fees and royalties on any product sales.

CELLTECH THERAPEUTICS LIMITED. In December 1999, we entered into a patent rights agreement with Celltech covering specified patents relating to humanized monoclonal antibodies. Under the agreement, Celltech paid us a \$3.0 million fee for the right to obtain worldwide licenses under our antibody humanization patents for up to three Celltech antibodies. We paid Celltech a fee for the right to obtain worldwide licenses under Celltech's antibody humanization patent for up to three of our antibodies. When a license is taken by either company, the other will be entitled to an additional license fee. Each company will pay royalties to the other on any sales of licensed antibodies.

TANOX, INC. In March 2000, we entered into a patent rights agreement with Tanox under our humanization patents. Tanox paid us a \$2.5 million fee, which reflected a \$1.5 million credit for a fee Tanox previously paid to us for a patent license for an antibody which was incorporated into this agreement. Tanox can obtain up to four patent licenses for humanized antibodies upon payment of an additional fee of at least \$1.0 million per antibody, as well as royalties on any product sales.

ELI LILLY AND COMPANY. In August and September 2000, we entered into two agreements to humanize antibodies for Lilly. Lilly agreed to pay us signing and licensing fees of \$1.7 million and \$1.36 million and to make additional payments upon the achievement of specified milestones and to pay royalties on any sales of the humanized antibodies.

OTHER PATENT LICENSE AGREEMENTS. We have entered into patent license agreements with a number of other companies that are independently developing humanized antibodies. In each license agreement, we granted a worldwide, exclusive or nonexclusive license under our patents to the other company for an antibody to a specific target antigen. In general, we received a licensing and signing fee and the right to receive annual maintenance fees and royalties on any product sales. Under some of these agreements, we also may receive milestone payments. In addition to Herceptin, we receive royalties on sales of Synagis, an antibody developed by MedImmune which is currently marketed in the U.S. and Europe, and expect to receive royalties on Mylotarg, an antibody developed by American Home Products which is currently marketed in the U.S. In addition to Genentech, MedImmune and American Home Products, we have patent license agreements with Sankyo, Biogen, IDEC Pharmaceuticals, Elan Pharmaceuticals, Medarex, SmithKline, Merck KGAA and Chugai.

MANUFACTURING AND FACILITIES

We own two buildings comprising approximately 92,000 square feet of research and development and general office space in Fremont, California. We relocated our California headquarters and research and development facilities to this space beginning in September 1998. We also lease an additional 43,000 square feet of laboratory and office space at the site of our former headquarters and research and development facilities in Mountain View, California. In 1998, we subleased all of that space to two other companies. The subleases are scheduled to terminate on December 31, 2000, the termination date of our lease with respect to that space.

We lease approximately 47,000 square feet of manufacturing, laboratory and office space in Plymouth, Minnesota. Our lease will terminate on February 29, 2004, subject to our options to extend the lease for two additional five year terms. Although these facilities are sufficient for our present manufacturing operations, in order to obtain regulatory approvals and to create capacity to produce our products for commercial sale at an acceptable cost, we will need to expand and improve our manufacturing capabilities. We intend to acquire additional space and construct a commercial manufacturing facility.

Of the products that we currently have in clinical development, Roche is responsible for manufacturing Zenapax, SmithKline is responsible for manufacturing the humanized anti-IL-4 antibody and Scil is responsible for manufacturing the SMART Anti-L-Selectin Antibody. We are responsible for manufacturing our other products for our own development. We intend to continue to manufacture potential products for use in preclinical and clinical trials in accordance with standard procedures that comply with appropriate regulatory standards.

PATENTS AND PROPRIETARY TECHNOLOGY

Our success depends significantly on our ability to obtain and maintain patent protection for our products and technologies, to preserve our trade secrets and to operate without infringing the proprietary rights of third parties. While we file and prosecute patent applications to protect our inventions, our pending patent applications may not result in the issuance of valid patents or our issued patents may not provide competitive advantages. Also, our patent protection may not prevent others from developing competitive products using related or other technology.

A number of companies, universities and research institutions have filed patent applications or received patents in the areas of antibodies and other fields relating to our programs. Some of these applications or patents may be competitive with our applications or contain material which could prevent the issuance of patents to us or result in a significant reduction in the scope of our issued patents.

The scope, enforceability and effective term of patents issued to companies, universities and research institutions can be highly uncertain and often involve complex legal and factual questions. No consistent policy has emerged regarding the breadth of claims in biotechnology patents, so that even issued patents may later be modified or revoked by the relevant patent authorities or courts. Moreover, the issuance of a patent in one country does not assure the issuance of a patent with similar claims in another country, and claim interpretation and infringement laws vary among countries, so we are unable to predict the extent of patent protection in any country.

We have been issued patents in the U.S., Europe and Japan which we believe cover many or most humanized antibodies. Some of these patents also cover other aspects of our SMART antibody technology. We have filed similar patent applications in other countries.

Our two humanization patents issued by the European Patent Office apply in the United Kingdom, Germany, France, Italy and eight other European countries. The European Patent Office procedures provide for an opposition period in which other parties may submit arguments as to why a patent was incorrectly granted and should be withdrawn or limited. Eighteen notices of opposition to our first European patent were filed during the opposition period for the patent, including oppositions by major pharmaceutical and biotechnology companies. At an oral hearing in March 2000, the Opposition Division of the European Patent Office decided to revoke the broad claims in our first European patent based on formal matters of European patent law, specifically that there had been an impermissible addition of subject matter after the filing of the original European patent application, but did not provide the rationale behind its decision. The decision upheld claims that protect Zenapax. The Opposition Division did not otherwise announce a decision on the issue of whether the claims in our patent are inventive in light of the prior art or other issues of patentability. We plan to appeal the Opposition Division's decision to the Technical Board of Appeal at the European Patent Office. The Technical Board of Appeal will consider all issues anew. The appeal suspends the decision of the Opposition Division during the appeals process, which is likely to take several vears.

The nine month opposition period for our second European antibody humanization patent ended in May 2000, and we have been advised that eight notices of opposition have been filed with respect to this patent. Also, three opposition statements were filed with the Japanese Patent Office with respect to our humanization patent issued in Japan in late 1998.

We intend to vigorously defend the European patents and the Japanese patent in these proceedings; however, we may not prevail in the opposition proceedings or any litigation contesting the validity of these patents. If our appeal with respect to our first European patent is unsuccessful or if the outcome of the other European or Japanese opposition proceedings or any litigation involving our antibody humanization patents were to be unfavorable, our ability to collect royalties on existing licensed products and to license our patents relating to humanized antibodies may be materially harmed.

In addition to seeking the protection of patents and licenses, we also rely upon trade secrets, know-how and continuing technological innovation which we seek to protect, in part, by confidentiality agreements with employees, consultants, suppliers and licensees. If these agreements are not honored, we might not have adequate remedies for any breach. Additionally, our trade secrets might otherwise become known or patented by our competitors.

GOVERNMENT REGULATION

The manufacturing, testing and marketing of our products are subject to regulation by numerous governmental authorities in the U.S. and other countries. In the U.S., pharmaceutical products are subject to rigorous FDA regulation. Additionally, other federal, state and local regulations govern the manufacture,

testing, clinical and nonclinical studies to assess safety and efficacy, approval, advertising and promotion of pharmaceutical products. The process of obtaining approval for a new pharmaceutical product or for additional therapeutic indications within this regulatory framework requires a number of years and the expenditure of substantial resources. Companies in the pharmaceutical and biotechnology industries, including us, have suffered significant setbacks in various stages of clinical trials, even in advanced clinical trials after promising results had been obtained in earlier trials.

In addition to the requirement for FDA approval of each pharmaceutical product, each pharmaceutical product manufacturing facility must be registered with, and approved by, the FDA. The manufacturing and quality control procedures must conform to rigorous guidelines in order to receive FDA approval. Pharmaceutical product manufacturing establishments are subject to inspections by the FDA and local authorities as well as inspections by authorities of other countries. To supply pharmaceutical products for use in the U.S., foreign manufacturing establishments must comply with these FDA approved guidelines. These foreign manufacturing establishments are subject to periodic inspection by the FDA or by corresponding regulatory agencies in these countries under reciprocal agreements with the FDA. Moreover, pharmaceutical product manufacturing facilities may also be regulated by state, local and other authorities.

For marketing of pharmaceutical products outside the U.S., we and our collaborative partners are subject to foreign regulatory requirements and, if the particular product is manufactured in the U.S., FDA and other U.S. export provisions. Requirements relating to the manufacturing, conduct of clinical trials, product licensing, promotion, pricing and reimbursement vary widely in different countries. Difficulties or unanticipated costs or price controls may be encountered by us or our licensees or marketing partners in our respective efforts to secure necessary governmental approvals. This could delay or prevent us or our licensees or our marketing partners from marketing potential pharmaceutical products.

Both before and after approval is obtained, a pharmaceutical product, its manufacturer and the holder of the Biologics License Application (BLA) for the pharmaceutical product are subject to comprehensive regulatory oversight. The FDA may deny a BLA if applicable regulatory criteria are not satisfied. Moreover, even if regulatory approval is granted, such approval may be subject to limitations on the indicated uses for which the pharmaceutical product may be marketed. Further, marketing approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems with the pharmaceutical product occur following approval. In addition, under a BLA, the manufacturer continues to be subject to facility inspection and the applicant must assume responsibility for compliance with applicable pharmaceutical product and establishment standards. Violations of regulatory requirements at any stage may result in various adverse consequences, which may include, among other adverse actions, withdrawal of the previously approved pharmaceutical product or marketing approvals and/or the imposition of criminal penalties against the manufacturer and/or BLA holders.

COMPETITION

Potential competitors have developed and are developing human and humanized antibodies or other compounds for treating autoimmune and inflammatory diseases, transplantation, asthma and cancers. In addition, a number of academic and commercial organizations are actively pursuing similar technologies, and several companies have developed or may develop technologies that may compete with our SMART antibody technology. Competitors may succeed in more rapidly developing and marketing technologies and products that are more effective than our products or that would render our products or technology obsolete or noncompetitive. Our collaborative partners may also independently develop products that are competitive with products that we have licensed to them. This could reduce our revenues under our agreements with these partners.

Any product that we or our collaborative partners succeed in developing and for which regulatory approval is obtained must then compete for market acceptance and market share. The relative speed with which we and our collaborative partners can develop products, complete the clinical testing and approval processes, and supply commercial quantities of the products to the market compared to competitive

companies will affect market success. For example, Novartis, which has a significant marketing and sales force directed to the transplantation market, has received approval to market Simulect, a product competitive with Zenapax, in the U.S. and Europe. Since Novartis launched Simulect in the European Union earlier than Roche, Zenapax may have a smaller market share than Simulect and other available products.

Other competitive factors include:

- the capabilities of our collaborative partners
- product efficacy and safety
- timing and scope of regulatory approval
- product availability, marketing and sales capabilities
- reimbursement coverage
- the amount of clinical benefit of our products relative to their cost
- method of and frequency of administration of our products
- price of our products, and
- patent protection of our products.

HUMAN RESOURCES

As of June 30, 2000, we had 298 full-time employees. Of the total, 106 employees were engaged in research and development, 50 in quality assurance and compliance, 52 in preclinical, clinical and regulatory, 32 in manufacturing and 58 in general and administrative functions. Our scientific staff members have diversified experience and expertise in molecular and cell biology, chemistry, microbiology, immunology, protein chemistry, computational chemistry and computer modeling. Our success will depend in large part on our ability to attract and retain skilled and experienced employees. None of our employees are covered by a collective bargaining agreement, and we consider our relations with our employees to be good.

MANAGEMENT

DIRECTORS AND EXECUTIVE OFFICERS

| NAME | AGE | TITLE |
|------------------------------|-----|---|
| | | |
| Laurence Jay Korn, Ph.D | 51 | Chief Executive Officer, Chairperson of the Board |
| Daniel J. Levitt, M.D., Ph.D | 52 | President, Research and Development |
| Douglas O. Ebersole, Esq | 44 | Senior Vice President, Legal and Licensing, General |
| | | Counsel and Secretary |
| Cary L. Queen, Ph.D | 50 | Senior Vice President and Vice President, Research, |
| | | Director |
| William R. Benjamin, Ph.D | 46 | Vice President, Drug Discovery |
| Christine C. Booker | 59 | Vice President, Quality and Compliance |
| Frances G. Charlson | 40 | Vice President, Human Resources |
| D. Scott Geyer | 46 | Vice President, Technical Development |
| Peter H. Grassam | 55 | Vice President, Manufacturing and General Manager, |
| | | Plymouth Facility |
| Robert L. Kirkman, M.D | 51 | Vice President, Business Development and Corporate |
| | | Communications |
| Corine K. Klingbeil, Ph.D | 46 | Vice President, Preclinical Development |
| Jaisim Shah | 40 | Vice President, Marketing |
| Jurgen Drews, M.D | 67 | Director |
| George M. Gould, Esq | 63 | Director |
| Max Link, Ph.D | 59 | Director |
| Jon S. Saxe, Esq | 64 | Director |

Laurence Jay Korn, Ph.D., has been a director and Chairperson of the Board since July 1986 and has served as Chief Executive Officer since January 1987. Previously, Dr. Korn headed a research laboratory and served on the faculty of the Department of Genetics at the Stanford University School of Medicine from March 1981 to December 1986. Dr. Korn received his Ph.D. from Stanford University and was a Helen Hay Whitney Postdoctoral Fellow at the Carnegie Institution of Washington and a Staff Scientist at the MRC Laboratory of Molecular Biology in Cambridge, England, before becoming an Assistant Professor at Stanford.

Daniel J. Levitt, M.D., Ph.D., has served as President, Research and Development since May 2000. From November 1996 to April 2000 he served as Senior Vice President, Clinical and Regulatory Affairs of the Company. From February 1995 to October 1996 he served as Vice President of Drug Development and Chief Medical Officer of Geron Corporation. From January 1990 until January 1995, Dr. Levitt held various positions at Sandoz Pharma Ltd., most recently as Worldwide Head of Oncology Clinical Research and Development. From 1986 to 1990, Dr. Levitt held various positions with Roche, including Director of Clinical Oncology and Immunology. He received post-graduate training at Yale-New Haven Hospital and the University of Alabama Birmingham Medical School. Dr. Levitt holds an M.D. and Ph.D. from the University of Chicago Pritzker School of Medicine.

Douglas O. Ebersole has served as our Senior Vice President, Legal and Licensing since April 1999. In addition, Mr. Ebersole has served as our Secretary since July 1992, and from July 1992 to April 1999 and again from April 2000, Mr. Ebersole served as our General Counsel. From April 1996 until April 1998, Mr. Ebersole served as Vice President, Licensing and Corporate Services, and from April 1998 to April 1999, he served as Senior Vice President, Legal, Licensing and Corporate Services, in addition to his positions as General Counsel and Secretary. Prior to joining us, he served first as Associate General Counsel and later as General Counsel at NeXT Computer. Prior to joining NeXT in 1989, he was a partner in the corporate department of the law firm Ware & Freidenrich. Mr. Ebersole received his J.D. from Stanford Law School.

Cary L. Queen, Ph.D., has been a director since January 1987 and has served as Vice President, Research, since April 1989 and as Senior Vice President since June 1993. Previously, Dr. Queen held positions at the National Institutes of Health from 1983 to 1986, where he studied the regulation of genes involved in the synthesis of antibodies. Dr. Queen received his Ph.D. in Mathematics from the University of California at Berkeley and subsequently served as an Assistant Professor of Mathematics at Cornell University.

William R. Benjamin, Ph.D., has served as our Vice President, Drug Discovery since July 1997. Prior to joining us, from November 1982 to June 1997, Dr. Benjamin was an employee of Roche, most recently serving as Vice President of Inflammation and Autoimmune Diseases. At Roche, Dr. Benjamin was responsible for leading the drug discovery activities of a multidisciplinary research department in the areas of inflammatory and immune-based diseases. From January 1981 to November 1982, Dr. Benjamin was a postdoctoral fellow at the National Institute of Dental Research at the National Institutes of Health. Dr. Benjamin received his Ph.D. degree from the University of South Florida, College of Medicine.

Christine C. Booker has served as our Vice President, Quality and Compliance since February 1996. Prior to joining us, from February 1995 through January 1996, Ms. Booker served as a consultant to us. From August 1994 to July 1996, Ms. Booker served as the principal consultant for Booker Associates. From March 1992 to October 1994, Ms. Booker served as Director, Quality Assurance for Synergen, Inc. From October 1980 to February 1992, Ms. Booker served in various positions at Genentech, including Associate Director, Technical Operations. Ms. Booker received her B.S. in Chemistry from DePaul University.

Frances G. Charlson has served as our Vice President, Human Resources since April 2000. In addition, Ms. Charlson has served in increasing positions of responsibility in our Human Resources Department since joining us in October 1992. Prior to joining the Company, she worked at Alza Corporation for six years in Human Resources and prior to joining Alza, she worked in Human Resources at Scios. Ms. Charlson is a Certified Compensation Professional from the American Compensation Association. Ms. Charlson received her B.S. in Public Relations from San Jose State University.

D. Scott Geyer has served as our Vice President, Technical Development since April 1998. Prior to that time, Mr. Geyer served as our Senior Director, Technical Operations from July 1997 to March 1998. Prior to joining us in July 1996, Mr. Geyer held various positions with the Ares-Serono Group from April 1987 to June 1996, most recently as Executive Director, Process Development at Ares Advanced Technology, Inc. Prior to that time, Mr. Geyer served in various positions at Ares Advanced Technology, Inc. from August 1994 to June 1996. Mr. Geyer received his B.S. in Microbiology from the University of Southwestern Louisiana and his M.S. in Veterinary Microbiology from Texas A&M University.

Peter H. Grassam has served as our Vice President, Manufacturing and General Manager of our Plymouth, Minnesota facility since January 1998. From September 1993 to January 1998, Mr. Grassam served as the Vice President of Operations and General Manager at the Smithfield site of Alpha Beta Technology, Inc., and as the Vice President of Operations at Serono Laboratories, Inc., from January 1992 to September 1993. Mr. Grassam received his Bachelor of Pharmacy from the University of London and received his post graduate certification at Groby Road Hospital in England. Mr. Grassam is a Member of the Royal Pharmaceutical Society of Great Britain and the American Pharmaceutical Association.

Robert L. Kirkman, M.D., has served as our Vice President, Business Development and Corporate Communications since July 1998. Prior to joining us, Dr. Kirkman served as the Chief of the Division of Transplantation at Brigham and Women's Hospital from 1992 to 1998. Dr. Kirkman was appointed to the position of Associate Professor of Surgery at Harvard Medical School from 1987 to 1998 and served as an Associate in Surgery at Massachusetts General Hospital from 1995 to 1998. Dr. Kirkman holds an M.D. from Harvard Medical School and received his post-graduate training at Peter Bent Brigham Hospital and Brigham and Women's Hospital.

Corine K. Klingbeil, Ph.D. has served as our Vice President, Preclinical Development since April 2000. Dr. Klingbeil joined us in January 1993 as Director, Preclinical Development until March 1995

when she became Senior Director. Dr. Klingbeil previously was department head and later Director, Preclinical Sciences and Development at Scios. After receiving her Ph.D. at the University of California at Santa Barbara, Dr. Klingbeil was a postdoctoral fellow at the University of California at San Francisco from 1983 to 1986.

Jaisim Shah has served as our Vice President, Marketing since August 2000. Prior to joining us, he served in various marketing management positions at Bristol Myers Squibb, most recently as Vice President, Marketing, for U.S. Pharmaceutical Group, Infectious Diseases. He joined Roche Laboratories in 1991 as Product Director for biotech oncology products for the U.S. market. He then became Global Business Leader for oncology and virology, based in Basel, Switzerland, for Roche in 1993. He received his MA in International Economics from the University of Akron and an MBA in Marketing from Oklahoma University.

Jurgen Drews, M.D., has been a director of the Company since February 1997. Since March 1998, Dr. Drews has served as a contributing advisor to OrbiMed Advisors. Dr. Drews served as President, Global Research and as a member of the Executive Committee of the Roche Group from January 1996 to December 1997. From January 1991 to December 1995, Dr. Drews served as President, International Research and Development and as a member of the Executive Committee for the Roche Group. Prior to that time, Dr. Drews served as Chairman of the Research Board and member of the Executive Committee for Roche from April 1986 to December 1990. Dr. Drews served as Head of International Pharmaceutical Research and Development for Sandoz from January 1982 to July 1985. Dr. Drews also serves as a director of MorphoSys GmbH, Genomics Pharmaceutical Company and Human Genome Sciences, Inc.

George M. Gould, Esq., has been a director of the Company since October 1989. Since June 1996, Mr. Gould has served as of counsel to the law firm Gibbons, Del Deo, Dolan, Griffinger & Vecchione. From May 1996 to December 1996, Mr. Gould was a Senior Vice President of PharmaGenics, Inc. Prior to that time Mr. Gould served as Vice President, Licensing & Corporate Development and Chief Patent Counsel for Roche from October 1989 to May 1996.

Max Link, Ph.D., has been a director of the Company since June 1993. Dr. Link served as the Chief Executive Officer of Boehringer Mannheim -- Therapeutics from October 1993 to May 1994 and as the Chief Executive Officer of Corange Ltd. from May 1993 to May 1994. Dr. Link served as the Chairman of Sandoz Pharma Ltd. from April 1992 to April 1993. Dr. Link served in various management positions at Sandoz Ltd. and Sandoz Pharmaceuticals Corporation from October 1971 to April 1992. Dr. Link is also a director of Access Pharmaceuticals, Inc., Alexion Pharmaceutical Inc., Cell Therapeutics, Inc., Cytrx Corp., Discovery Laboratories, Inc., Human Genome Sciences, Inc., Osiris Therapeutics, Inc. and Celsion Corporation.

Jon S. Saxe, Esq., has been a director of the Company since March 1989. From January 1995 to April 1999, Mr. Saxe served as President of the Company. Since May 2000, Mr. Saxe has served as a consultant to us. From May 1999 to April 2000, Mr. Saxe served as Senior Advisor to the Chief Executive Officer of the Company. Mr. Saxe was a consultant to the Company from June 1993 to December 1994. He has served as President of Saxe Associates since May 1993. Mr. Saxe is also a director of Incyte Genomics Inc., Questcor, Inc., First Horizon Pharmaceuticals, Inc., InSite Vision, Inc., SciClone Pharmaceuticals, Inc. and ID Biomedical Corporation and three private companies. Mr. Saxe received his B.S.Ch.E. from Carnegie-Mellon University, his J.D. from George Washington University School of Law and his LL.M. from New York University School of Law.

DESCRIPTION OF CAPITAL STOCK

This summary does not purport to be complete and is subject to, and qualified in its entirety by, the provisions of our certificate of incorporation, as amended, and all applicable provisions of Delaware law.

GENERAL

We are authorized to issue 90,000,000 shares of common stock, \$.01 par value, and 10,000,000 shares of preferred stock, \$.01 par value.

COMMON STOCK

As of June 30, 2000, we had issued and outstanding approximately 39,849,124 shares of common stock held of record by approximately 125 stockholders. Holders of common stock are entitled to one vote per share for the election of directors and all other matters submitted to a vote of our stockholders. Subject to the rights of any holders of preferred stock that may be issued in the future, the holders of common stock are entitled to share ratably in such dividends as may be declared by our board of directors out of funds legally available therefor. In the event of our dissolution, liquidation or winding up, holders of common stock are entitled to share ratably in all assets remaining after payment of all liabilities and liquidation preferences of any preferred stock. Holders of common stock have no preemptive, subscription, redemption, conversion rights or similar rights. Our certificate of incorporation does not provide for cumulative voting rights with respect to the election of directors. All outstanding common stock is fully paid and nonassessable. Shares of our common stock are reserved for issuance under our option and employee stock purchase plans, and there are options outstanding under our stock plans for shares of common stock.

PREFERRED STOCK

Our board of directors has the authority, without any action by our stockholders, to issue preferred stock in one or more series with such designations, rights and preferences (including dividend, conversion, voting or other rights or liquidation preferences) as determined by our board of directors. The issuance of preferred stock could delay, defer or prevent a change of control and could decrease the amount of earnings and assets available for distribution to, or adversely affect the voting power or other rights of, holders of common stock. In addition, the issuance of preferred stock could have the effect of decreasing the market price of our common stock. At present, there are no shares of preferred stock outstanding.

TRANSFER AGENT

The transfer agent for our common stock is ChaseMellon Shareholder Services, LLC. Its address is 235 Montgomery Street, 23rd Floor, San Francisco, California 94104. Its telephone number is (415) 743-1444.

UNDERWRITING

Under the terms and subject to the conditions contained in an underwriting agreement, dated , 2000, we have agreed to sell to the underwriters named below, for whom Credit Suisse First Boston Corporation, CIBC World Markets Corp. and SG Cowen Securities Corporation are acting as representatives, the following respective numbers of shares of our common stock:

| UNDERWRITER | NUMBER OF SHARES |
|--|---------------------|
| Credit Suisse First Boston Corporation CIBC World Markets Corp | |
| Total | 3,000,000 |

The underwriting agreement provides that the underwriters are obligated to purchase all the shares of common stock in the offering if any are purchased, other than those shares covered by the over-allotment option described below. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may be increased or the offering may be terminated.

We have granted to the underwriters a 30-day option to purchase on a pro rata basis up to 450,000 additional shares from us at the public offering price less the underwriting discounts and commissions. The option may be exercised only to cover any over-allotments of common stock.

The underwriters propose to offer the shares of common stock initially at the offering price on the cover page of this prospectus and to selling group members at that price less a selling concession of \$ per share. The underwriters and selling group members may allow a discount of \$ per share on sales to other broker/dealers. After the initial public offering, the public offering price and concession and discount to broker/dealers may be changed by the representatives.

The following table summarizes the compensation and estimated expenses we will pay:

| | PER S | HARE | TOTAL | | | | |
|---|---------------------------|------------------------|---------------------------|------------------------|--|--|--|
| | WITHOUT OVER-ALLOTMENT | WITH OVER-ALLOTMENT | WITHOUT OVER-ALLOTMENT | WITH OVER-ALLOTMENT | | | |
| Underwriting Discounts and Commissions paid by us Expenses, payable by us | \$ | \$ | \$ | \$ | | | |

We have agreed that we will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, or file with the Securities and Exchange Commission a registration statement under the Securities Act relating to any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, without the prior written consent of Credit Suisse First Boston Corporation for a period of 90 days after the date of this prospectus, except issuances of shares of our common stock pursuant to the conversion of convertible or exchangeable securities or the exercise of warrants or options, in each case outstanding on the date of this prospectus, grants of employee stock options pursuant to the terms of a plan in effect on the date of this prospectus, or issuances of shares of our common stock pursuant to the exercise of such options.

All of our executive officers and directors have agreed that they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, enter into a transaction which would have the same effect, or enter into any swap, hedge or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock, whether any of these transactions are to be settled by delivery of our common stock or other securities, in cash or otherwise, or publicly disclose the intention to make any offer, sale, pledge or disposition, or to

enter into any of these types of transactions, swap, hedge or other arrangement, without, in each case, the prior written consent of Credit Suisse First Boston Corporation for a period of 60 days after the date of this prospectus.

We have agreed to indemnify the underwriters against liabilities under the Securities Act or contribute to payments which the underwriters may be required to make in that respect.

In connection with the offering the underwriters may engage in stabilizing transactions, over-allotment transactions, syndicate covering transactions, penalty bids and passive market making in accordance with Regulation M under the Exchange Act.

- Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.
- Over-allotment transactions involve sales by the underwriters of shares in excess of the number of shares the underwriters are obligated to purchase, which creates a syndicate short position. The short position may be either a covered short position or a naked short position. In a covered short position, the number of shares over-alloted by the underwriters is not greater than the number of shares that they may purchase in the over-allotment option. In a naked short position, the number of shares involved is greater than the number of shares in the over-allotment option. The underwriters may close out any short position by either exercising their over-allotment option and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of the common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. If the underwriters sell more shares than could be covered by the over-allotment option -- a naked short position -- that position can only be closed out by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.
- Penalty bids permit the representatives to reclaim a selling concession from a syndicate member when the common stock originally sold by the syndicate member is purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.
- In passive market making, market makers in the common stock who are underwriters or prospective underwriters may, subject to limitations, make bids for or purchases of the common stock until the time, if any, at which a stabilizing bid is made.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock. As a result, the price of the common stock may be higher than the price that might otherwise exist in the open market. These transactions may be effected on The Nasdaq Stock Market's National Market or otherwise and, if commenced, may be discontinued at any time.

A prospectus in electronic format may be made available on the Web sites maintained by one or more of the underwriters participating in this offering. The representatives may agree to allocate a number of shares to underwriters for sale to their online brokerage account holders. Internet distributions will be allocated by the underwriters that will make internet distributions on the same basis as other allocations.

NOTICE TO CANADIAN RESIDENTS

RESALE RESTRICTIONS

The distribution of the common stock in Canada is being made only on a private placement basis exempt from the requirement that we prepare and file a prospectus with the securities regulatory authorities in each province where trades of common stock are made. Any resale of the common stock in Canada must be made under applicable securities laws which will vary depending on the relevant jurisdiction, and which may require resales to be made under available statutory exemptions or under a discretionary exemption granted by the applicable Canadian securities regulatory authority. Purchasers are advised to seek legal advice prior to any resale of the common stock.

REPRESENTATIONS OF PURCHASERS

By purchasing common stock in Canada and accepting a purchase confirmation, a purchaser is representing to us and the dealer from whom the purchase confirmation is received that:

- the purchaser is entitled under applicable provincial securities laws to purchase such common stock without the benefit of a prospectus qualified under those securities laws
- where required by law, the purchaser is purchasing as principal and not as agent, and
- the purchaser has reviewed the text above under "Resale Restrictions."

RIGHTS OF ACTION (ONTARIO PURCHASERS)

The securities being offered are those of a foreign issuer and Ontario purchasers will not receive the contractual right of action prescribed by Ontario securities law. As a result, Ontario purchasers must rely on other remedies that may be available, including common law rights of action for damages or rescission or rights of action under the civil liability provisions of the U.S. federal securities laws.

ENFORCEMENT OF LEGAL RIGHTS

All of the issuer's directors and officers as well as the experts named herein may be located outside of Canada and, as a result, it may not be possible for Canadian purchasers to effect service of process within Canada upon the issuer or such persons. All or a substantial portion of the assets of the issuer and such persons may be located outside of Canada and, as a result, it may not be possible to satisfy a judgment against the issuer or such persons in Canada or to enforce a judgment obtained in Canadian courts against such issuer or persons outside of Canada.

NOTICE TO BRITISH COLUMBIA RESIDENTS

A purchaser of common stock to whom the Securities Act, British Columbia, applies is advised that such purchaser is required to file with the British Columbia Securities Commission a report within ten days of the sale of any common stock acquired by the purchaser pursuant to this offering. The report must be in the form attached to British Columbia Securities Commission Blanket Order BOR #95/17, a copy of which may be obtained from us. Only one report must be filed for common stock acquired on the same date and under the same prospectus exemption.

TAXATION AND ELIGIBILITY FOR INVESTMENT

Canadian purchasers of common stock should consult their own legal and tax advisors about the tax consequences of an investment in the common stock in their particular circumstances and about the eligibility of the common stock for investment by the purchaser under relevant Canadian legislation.

LEGAL MATTERS

The validity of the issuance of the common stock offered hereby will be passed upon by Gray Cary Ware & Freidenrich LLP, Palo Alto, California. Certain legal matters in connection with this offering will be passed upon for the underwriters by Skadden, Arps, Slate, Meagher & Flom LLP, Palo Alto, California.

EXPERTS

Ernst & Young LLP, independent auditors, have audited our consolidated financial statements appearing in our Annual Report on Form 10-K for the year ended December 31, 1999, as set forth in their report thereon. We have incorporated our financial statements by reference in reliance upon Ernst & Young LLP's report given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. In connection with this offering we have filed with the SEC a registration statement under the Securities Act of 1933 relating to the common stock we are offering. As permitted by the SEC rules, this prospectus omits certain information included in the registration statement. For a more complete understanding of our common stock and this offering, you should refer to the registration statement, including its exhibits.

The SEC allows us to "incorporate by reference" the information we file with it, which means we can disclose important information to you by referring you to those documents. The information included in the following documents is incorporated by reference and is considered to be a part of this prospectus. The most recent information that we file with the SEC automatically updates and supersedes older information. We have previously filed the following reports with the SEC and are incorporating them by reference into this prospectus:

- 1. Our Annual Report on Form 10-K for the year ended December 31, 1999;
- 2. Our Quarterly Reports on Forms 10-Q for the quarters ended March 31, 2000 and June 30, 2000;
- 3. Our Current Reports on Form 8-K filed on February 14, 2000, March 1, 2000 and August 29, 2000; and
- 4. The description of our common stock included in our Registration Statement on Form 8-A filed on December 23, 1991, and any amendments or reports filed for the purpose of updating that description.

We also automatically incorporate by reference all documents we file pursuant to Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 both (a) after the date of the initial registration statement of which this prospectus forms a part and prior to the effectiveness of that registration statement, and (b) after the effectiveness of the registration statement of which this prospectus forms a parts and before all of the shares registered under that registration statement are sold.

We will provide without charge, to each person who receives a prospectus, a copy of the information that has been incorporated by reference in this prospectus. If you would like to obtain this information from us, please direct your request to us in writing at Protein Design Labs, Inc. Attn: Corporate Communications, 34801 Campus Drive, Fremont, California 94555 or contact us by telephone at (510) 574-1400.

The registration statement can also be inspected and copied at prescribed rates at the public reference facilities maintained by the SEC at Room 1024, 450 Fifth Street, N.W., Washington, D.C. 20549, and at the SEC regional offices at Seven World Trade Center, 13th Floor, New York, New York 10048 and Northwestern Atrium Center, 500 West Madison Street, Suite 1400, Chicago, Illinois 60661. You may obtain information regarding the Washington, D.C. Public Reference Room by calling the SEC at 1-800-SEC-0330. In addition, the registration statement is publicly available through the SEC's site on the World Wide Web, located at http://www.sec.gov. In addition, you may read and copy our SEC filings at the office of the National Association of Securities Dealers, Inc. at 1735 K Street, N.W., Washington, D.C. 20006.

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PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.

The following table sets forth the fees and expenses in connection with the issuance and distribution of the securities being registered hereunder. Except for the SEC registration, the Nasdaq Listing Fee and the NASD filing fee, all amounts are estimates.

| SEC registration fee | \$ 93,471 |
|---|-----------|
| Nasdaq Listing Fee | 17,500 |
| NASD filing fee | 35,906 |
| Accounting fees and expenses | 60,000 |
| Legal fees and expenses | 130,000 |
| Blue Sky fees and expenses (including counsel fees) | 1,000 |
| Printing and engraving expenses | 125,000 |
| Transfer agent's and registrar's fees and expenses | 1,000 |
| Miscellaneous expenses, including listing fees | 36,123 |
| | |
| Total | \$500,000 |

ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

Section 145 of the Delaware General Corporation Law ("DGCL") authorizes a court to award, or a corporation's board of directors to grant, indemnity to directors and officers under certain circumstances for liabilities incurred in connection with their activities in such capacities (including reimbursement for expenses incurred). The Registrant's Restated Certificate of Incorporation provides that the Registrant will indemnify its directors and officers to the fullest extent permitted by law and that directors shall not be liable for monetary damages to the Registrant or its stockholders for breach of fiduciary duty, except to the extent that the DGCL prohibits elimination or limitation of such liability.

The Registrant's Restated Certificate of Incorporation provides that no director of the Registrant will be personally liable to the Registrant or its stockholders for monetary damages for breach of fiduciary duty as a director, except for liability (i) for any breach of the director's duty of loyalty to the Registrant or to its stockholders, (ii) for acts or omissions not made in good faith or involving intentional misconduct or a knowing violation of the law, (iii) under Section 174 of the DGCL, or (iv) for any transactions from which the director derives an improper personal benefit. In addition, the Registrant's Amended and Restated Bylaws provide that any director or officer who was or is a party or is threatened to be made a party to any action or proceeding by reason of his or her services to the Registrant will be indemnified to the fullest extent permitted by the DGCL.

The Registrant has entered into agreements with each of its executive officers and directors under which the Registrant has agreed to indemnify each of them against expenses and losses incurred for claims brought against them by reason of their being an officer or director of the Registrant. There is no pending litigation or proceeding involving a director or officer of the Registrant as to which indemnification is being sought, nor is the Registrant aware of any pending or threatened litigation that may result in claims for indemnification by any director or executive officer.

ITEM 16. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES.

Exhibits:

| EXHIBIT NUMBER | DESCRIPTION |
|-------------------|---|
| 1.1* | Form of Underwriting Agreement |
| 5.1 | Opinion of Gray Cary Ware & Freidenrich LLP |
| 23.1 | Consent of Gray Cary Ware & Freidenrich LLP (contained in |
| | Exhibit 5.1) |
| 23.2 | Consent of Ernst & Young LLP, independent auditors |
| 24.1* | Power of Attorney |
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* Previously filed.

ITEM 17. UNDERTAKINGS.

- (a) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement 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.
- (b) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, 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, 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.
 - (c) The undersigned registrant hereby undertakes that:
 - (1) For purposes of determining any liability under the Securities Act of 1933, 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 of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered herein, 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, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Amendment No. 1 to registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the County of Alameda, State of California on September 25, 2000.

PROTEIN DESIGN LABS, INC.

By: /s/ LAURENCE JAY KORN

Laurence Jay Korn Chief Executive Officer and Chairperson of the Board of Directors

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 1 to Registration Statement has been signed by the following persons in the

capacities and on the dates indicated.

Date: September 25, 2000 /s/ LAURENCE JAY KORN

Laurence Jay Korn Chief Executive Officer and

Chairperson of the Board of Directors (Principal

Executive Officer)

Date: September 25, 2000 ROBERT L. KIRKMAN*

Robert L. Kirkman Vice President, Business Development

and Corporation Communications (Principal Accounting

Officer)

Date: September 25, 2000 JON S. SAXE*

Jon S. Saxe Director

| Date: September 25, 2000 | CARY L. QUEEN* |
|--------------------------|---------------------------------------|
| | Cary L. Queen Director |
| Date: September 25, 2000 | GEORGE M. GOULD* |
| | George M. Gould Director |
| Date: September 25, 2000 | MAX LINK* |
| | Max Link Director |
| Date: September 25, 2000 | JURGEN DREWS* |
| | Jurgen Drews Director |
| Date: September 25, 2000 | *By: /s/ LAURENCE JAY KORN |
| | Laurence Jay Korn Attorney-in-Fact |

INDEX TO EXHIBITS

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| 23.2 | Consent of Ernst & Young LLP, independent auditors |
| 24.1* | Power of Attorney |
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 $^{^{\}star}$ Previously filed.

September 25, 2000

Securities and Exchange Commission Judiciary Plaza 450 Fifth Street, N.W. Washington, D.C. 20549

Ladies and Gentlemen:

As counsel to Protein Design Labs, Inc. a Delaware corporation (the "Company"), we are rendering this opinion in connection with the filing of a Registration Statement on Form S-3 (the "Registration Statement") with the Securities and Exchange Commission covering the offering of up to 3,450,000 shares of the Company's Common Stock, \$.01 par value, together with any additional shares covered by a registration statement filed pursuant to Rule 462 (collectively, the "Shares"). We have examined all instruments, documents and records which we deemed relevant and necessary for the basis of our opinion hereinafter expressed. In such examination, we have assumed the genuineness of all signatures and the authenticity of all documents submitted to us as originals and the conformity to the originals of all documents submitted to us as copies.

We express no opinion with respect to (i) the availability of equitable remedies, including specific performance, or (ii) the effect of bankruptcy, insolvency, reorganization, moratorium or equitable principles relating to or limiting creditors' rights generally.

Based on such examination, we are of the opinion that the Shares, when issued and sold in accordance with the Registration Statement, will be duly authorized, legally issued, fully paid and nonassessable.

We hereby consent to the filing of this opinion as an exhibit to the above-referenced Registration Statement and any registration statement filed pursuant to Rule 462 and to the use of our name wherever it appears in said Registration Statement and any registration statement filed pursuant to Rule 462, including the Prospectuses constituting a part thereof, as originally filed or as subsequently amended.

Respectfully submitted,

/s/ Gray Cary Ware & Freidenrich LLP

GRAY CARY WARE & FREIDENRICH LLP

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the reference to our firm under the captions "Selected Financial Data" and "Experts" in Amendment No. 1 to the Registration Statement (Form S-3 No. 333-44754) and related Prospectus of Protein Design Labs, Inc. for the registration of 3,450,000 shares of its common stock and to the incorporation by reference therein of our report dated February 1, 2000 with respect to the consolidated financial statements of Protein Design Labs, Inc. included in its Annual Report on Form 10-K for the year needed December 31, 1999, filed with the Securities and Exchange Commission.

/s/ ERNST & YOUNG LLP

Palo Alto, California September 25, 2000