

REGISTRATION NO.

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 20549

FORM S-3  
REGISTRATION STATEMENT  
UNDER  
THE SECURITIES ACT OF 1933

REGENERON PHARMACEUTICALS, INC.  
(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

NEW YORK  
(STATE OR OTHER JURISDICTION OF  
INCORPORATION OR ORGANIZATION)

13-3444607  
(I.R.S. EMPLOYER  
IDENTIFICATION NO.)

777 OLD SAW MILL RIVER ROAD  
TARRYTOWN, NEW YORK 10591-6707  
(914) 347-7000

(ADDRESS, INCLUDING ZIP CODE AND TELEPHONE NUMBER, INCLUDING AREA CODE, OF  
REGISTRANT'S PRINCIPAL EXECUTIVE OFFICES)

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AGENT FOR SERVICE)

COPIES TO:

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APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC: As soon as  
practicable after this Registration Statement becomes effective.

If the only securities being registered on this form are being offered  
pursuant to dividend or interest reinvestment plans, please check the following  
box. [ ]

If any of the securities being registered on this Form are to be offered on  
a delayed or continuous basis pursuant to Rule 415 under the Securities Act of  
1933, other than securities offered only in connection with dividend or interest  
reinvestment plans, check the following box. [ ]

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

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

If delivery of the prospectus is expected to be made pursuant to Rule 434,  
please check the following box. [ ]

CALCULATION OF REGISTRATION FEE

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	AMOUNT TO BE REGISTERED(1)	PROPOSED MAXIMUM OFFERING PRICE PER UNIT(2)	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE(2)	AMOUNT OF REGISTRATION FEE(2)
Common stock \$0.001 par value (including the associated Rights to purchase Series A Junior Participating Preferred Stock)(3)...	4,600,000	\$34.477	\$158,594,200	\$39,648.55

(1) Includes 600,000 shares of common stock of the Registrant which may be sold

pursuant to an option granted to the Underwriters to cover over-allotments.

- (2) Estimated solely for the purpose of computing the amount of the registration fee pursuant to Rule 457(c) under the Securities Act of 1933, as amended, based on the average of the high and low price of the common stock reported on the Nasdaq National Market on January 22, 2001.
- (3) The Rights to purchase shares of our Series A Junior Participating Preferred Stock initially are attached to and trade with the shares of our common stock being registered hereby. Value attributed to such Rights, if any, is reflected in the market price of our common stock.

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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 SPECIFICALLY STATING THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(a) OF THE SECURITIES ACT OF 1933 OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE COMMISSION, ACTING PURSUANT TO SAID SECTION 8(a), MAY DETERMINE.

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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  
PRELIMINARY PROSPECTUS DATED JANUARY 25, 2001

PROSPECTUS

4,000,000 SHARES

REGENERON PHARMACEUTICALS, INC.

COMMON STOCK

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Regeneron is selling 4,000,000 shares.

The shares are quoted on the Nasdaq National Market under the symbol "REGN." On January 24, 2001, the last sale price of the shares as reported on the Nasdaq National Market was \$37.125 per share.

INVESTING IN THE COMMON STOCK INVOLVES RISKS THAT ARE DESCRIBED IN THE "RISK FACTORS" SECTION BEGINNING ON PAGE 6 OF THIS PROSPECTUS.

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	PER SHARE	TOTAL
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Public offering price.....	\$	\$
Underwriting discount.....	\$	\$
Proceeds, before expenses, to Regeneron.....	\$	\$

The underwriters may also purchase up to 600,000 additional shares from Regeneron at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus to cover over-allotments.

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.

The shares will be ready for delivery on or about \_\_\_\_\_, 2001.

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MERRILL LYNCH & CO.

JP MORGAN

ROBERTSON STEPHENS

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The date of this prospectus is \_\_\_\_\_, 2001.

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In this prospectus, "Regeneron," "our company," "we," "us," "the issuer," "the registrant," and "our" refer to Regeneron Pharmaceuticals, Inc. You should rely only on the information contained or incorporated by reference in this prospectus. We have not, and the underwriters have not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus is accurate only as of the date on the front cover of this prospectus. Our business, financial condition, results of operations, and prospects may have changed since that date.

## SUMMARY

The following summary highlights information contained in other parts of this prospectus or incorporated by reference in this prospectus. You should read this summary together with the more detailed information elsewhere in this prospectus and in our financial statements and accompanying notes and other information incorporated by reference in this prospectus. Unless otherwise indicated, all information in this prospectus assumes no exercise of the underwriters' over-allotment option, gives no effect to the exercise of outstanding options and warrants to purchase common stock, and assumes all share numbers set forth in this prospectus are as of January 23, 2001.

## REGENERON PHARMACEUTICALS, INC.

We are a biopharmaceutical company that discovers, develops and intends to commercialize therapeutic drugs for the treatment of serious medical conditions. Our product pipeline includes product candidates for the treatment of obesity, rheumatoid arthritis and other inflammatory conditions, cancer and related disorders, allergies, asthma, and other diseases and disorders.

Our core business strategy is to combine our strong foundation in science and technology with state-of-the-art manufacturing and clinical development capabilities to build a successful, integrated biopharmaceutical company. Our efforts have yielded a diverse and growing pipeline of product candidates that have the potential to address a variety of unmet medical needs. A key aspect of our strategy is to retain significant ownership and commercialization rights to our pipeline. The ability to participate in the commercialization of our products will enable us to retain the majority of the potential economic rewards from discovering and developing our pipeline. Longer-term, we will continue to invest in the development of additional enabling technologies to assist in our efforts to identify, develop, and commercialize new product candidates.

Below is a summary of our leading clinical programs, as well as several product candidates that are expected to enter clinical trials over the next two years. We retain sole ownership and marketing rights for each of these programs and currently are developing them independently of any corporate partners.

- AXOKINE(R): Acts on the brain region regulating food intake and energy expenditure and is being developed for the treatment of obesity. In November 2000, we announced the preliminary results of a twelve-week Phase II dose-ranging trial of AXOKINE in 170 severely obese patients. In the trial, AXOKINE was generally well tolerated and patients treated with AXOKINE showed medically meaningful and statistically significant weight loss compared to those receiving placebo. Patients who received the optimal dose of 1 mcg/kg averaged 10 pounds more weight loss than patients on placebo and continued to lose weight over the entire twelve-week treatment period. Subject to discussions with the FDA, we intend to initiate Phase III testing of AXOKINE in severely obese patients in mid-2001.
- PEGYLATED AXOKINE: Chemically modified version of AXOKINE that is being developed as a more potent, long-acting form of the protein. Pegylated AXOKINE may allow for less frequent and/or lower dosing in patients. Pegylated AXOKINE currently is in late-stage preclinical development and we anticipate initiating a Phase I clinical trial in mid-2001.
- INTERLEUKIN-1 CYTOKINE TRAP (IL-1 TRAP): Protein-based antagonist for the interleukin-1 (called IL-1) cytokine. IL-1 is thought to play a major role in rheumatoid arthritis and other inflammatory diseases. In December 2000, we initiated a Phase I study to assess the safety and tolerability of the IL-1 Trap in patients with rheumatoid arthritis. The placebo-controlled, double-blind, dose-escalation study is being conducted at several centers in the United States and includes a single dose phase and a multiple dose phase. We expect the study to be completed in the second half of 2001.
- INTERLEUKIN-4/INTERLEUKIN-13 CYTOKINE TRAP (IL-4/IL-13 TRAP): Protein-based antagonist for the interleukin-4 and interleukin-13 (called IL-4 and IL-13) cytokines. These cytokines are thought to play a major role in diseases such as asthma, allergic disorders and other

inflammatory diseases. We expect to initiate a Phase I clinical trial of a dual IL-4/IL-13 Trap for asthma/allergy related conditions in late 2001.

- VEGF TRAP: Protein-based antagonist to Vascular Endothelial Growth Factor (called VEGF, also known as Vascular Permeability Factor or VPF), which is required for the growth of blood vessels that are needed for tumors to grow and is a potent regulator of vascular permeability and leaks. In multiple preclinical models of cancer, the VEGF Trap blocked the growth of tumors by an anti-angiogenesis mechanism. Also in preclinical models, the VEGF Trap blocked vascular leaks caused by VEGF. The VEGF Trap is a potential treatment for harmful angiogenesis or vascular leak in settings of cancer and other conditions and is expected to enter Phase I clinical trials in mid-2001.
- ANGIOPOIETINS: A new family of growth factors that act specifically on the endothelium cells that line blood vessels. Angiopoietins, and engineered forms of these growth factors that can act as activators and blockers, are in preclinical testing for promoting blood vessel growth (to provide blood flow in diseased hearts and other tissues that have lost their original blood supplies), for blocking blood vessel growth (for the treatment of cancers) and for fixing leaky blood vessels that cause swelling and edema in many different diseases such as stroke, diabetic retinopathy and inflammatory diseases.

In addition, we are conducting research with The Procter & Gamble Company in muscle diseases and other fields. We are also collaborating with Medarex, Inc. to discover, develop and commercialize certain human antibodies as therapeutics. In partnership with Amgen Inc., we are conducting clinical trials with Neurotrophin-3, or NT-3, for the treatment of constipating conditions. In all of these research collaborations, we retain 50% of the commercialization rights. Following a review of available clinical trial data, we and Amgen recently discontinued the development of Brain-Derived Neurotrophic Factor (BDNF) for the treatment of amyotrophic lateral sclerosis (ALS).

Our ability to develop product candidates results from the application of our technology platforms. In contrast to basic genomics approaches, which attempt to identify every gene in a cell or genome, our technology platforms are designed to discover specific genes of therapeutic interest for a particular disease or cell type. Using these technologies, we have discovered new families of growth factors and receptors, which have led to multiple product candidates. In the area of cytokine antagonists, our technology platforms have already produced more than 10 patented proteins, including the IL-1 Trap currently in Phase I clinical testing, and several others which are in preclinical development.

We believe that our manufacturing facilities in Tarrytown, New York and Rensselaer, New York will give us an advantage in positioning ourselves to commercialize product candidates. The advancement of product candidates through preclinical and clinical development requires process development, scale-up, and manufacturing expertise. We have made a substantial investment to develop these capabilities internally to support our clinical and preclinical programs and help better position us for the potential commercialization of our product candidates in accordance with the requirements of the Food and Drug Administration (the FDA). Currently, we dedicate approximately 200 people to these manufacturing activities. At our 100,000 square foot Rensselaer facility and our 8,000 square foot Tarrytown facility, we manufacture drugs for our preclinical and clinical studies. At our Rensselaer facility, we also manufacture a product for Merck & Co., Inc. under a long-term contract. We will continue to upgrade and expand our manufacturing facilities as we advance our product candidates toward commercialization.

Our intellectual property portfolio includes 45 issued U.S. patents and more than 100 pending applications in all key areas of our research and development, including AXOKINE, Cytokine Traps, angiogenesis, bone and cartilage formation, muscle atrophy, and neurological disorders. We have a policy of filing patent applications to protect technology, inventions, and improvements we consider important to the development of our business. We also rely on trade secrets, know-how, and continuing technological innovation to maintain and enhance our competitive position.

Each member of our senior management team has significant experience in the biopharmaceutical industry. In addition, our Board of Directors consists of noted business and scientific leaders, including P. Roy Vagelos, M.D., the former Chairman and CEO of Merck & Co., Inc. and three Nobel Laureates. In a 1997 survey by the Institute for Scientific Information, our Chief Scientific Officer, George D. Yancopoulos, M.D., Ph.D., was listed among the 11 most highly cited scientists and was the only non-academic scientist in the group. We believe that we have been successful in attracting skilled and experienced personnel in a highly competitive environment. As of December 31, 2000, we had 491 full-time employees, 85 of whom hold a Ph.D. or M.D. degree or both.

#### RECENT OPERATING RESULTS

On January 25, 2001, we announced our full year and fourth quarter financial and operating results for 2000. We reported a net loss of \$23.2 million, or \$0.66 per share, for the year ended December 31, 2000, compared to a net loss of \$23.1 million, or \$0.74 per share, in 1999. Cash and marketable securities at December 31, 2000 were \$154.4 million, compared to \$93.6 million at December 31, 1999. Our total revenue for 2000 increased to \$67.8 million from \$39.7 million in 1999. The increase in total revenue was due primarily to higher contract research and development revenue, higher contract manufacturing revenue, and research progress payments received in 2000. Our full year operating expenses in 2000 increased to \$89.4 million from \$62.8 million in 1999 due primarily to higher research and development and contract manufacturing expenses.

For the fourth quarter of 2000, we reported a net loss of \$8.5 million, or \$0.23 per share, compared to a net loss of \$1.4 million, or \$0.04 per share, in the fourth quarter of 1999. Our total revenue in the fourth quarter of 2000 increased to \$21.7 million from \$13.1 million in the same period of 1999 due primarily to higher contract manufacturing revenue. Total operating expenses increased to \$30.1 million in the fourth quarter of 2000 from \$14.5 million in the same period in 1999 due primarily to higher research and development and contract manufacturing expenses.

During the fourth quarter of 2000, we adopted Staff Accounting Bulletin 101, Revenue Recognition in Financial Statements, (SAB 101) effective as of January 1, 2000. The cumulative effect of adopting SAB 101 was to increase our net loss by \$1.6 million, or \$0.04 per share, for the full year 2000.

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We are a New York corporation organized on January 8, 1988. Our executive offices are at 777 Old Saw Mill River Road, Tarrytown, NY 10591-6707 and our telephone number is (914) 347-7000.

## THE OFFERING

Common stock offered..... 4,000,000 shares

Shares outstanding after the offering:

Common stock..... 38,215,308 shares  
 Class A stock..... 2,612,845 shares  
 Total..... 40,828,153 shares

Holder of our Class A stock are entitled to ten votes per share and the holders of our common stock are entitled to one vote per share.

Use of proceeds..... We will receive net proceeds from this offering of approximately \$140.4 million, assuming a public offering price of \$37.125 per share. We intend to use the net proceeds for research and development, commercialization expenses, capital expenditures, potential acquisitions, working capital, and other general corporate purposes. See "Use of Proceeds."

Risk factors..... See "Risk Factors" and other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.

Nasdaq National Market symbol..... REGN

The number of shares outstanding after the offering is as of January 23, 2001 and excludes (1) options to purchase 7,520,327 shares of our common stock under our 1990 Long-Term Incentive Plan and 2000 Long-Term Incentive Plan, of which 2,770,863 were exercisable at January 23, 2001 and (2) 107,400 warrants held by Medtronic, Inc. as of January 23, 2001.

## SUMMARY SELECTED FINANCIAL DATA

	NINE MONTHS ENDED SEPTEMBER 30,		YEAR ENDED DECEMBER 31,				
	2000	1999	1999	1998	1997	1996	1995
(IN THOUSANDS, EXCEPT PER SHARE DATA)							
STATEMENT OF OPERATIONS DATA:							
Revenues:							
Contract research and development.....	\$ 27,043	\$ 15,311	\$ 24,539	\$19,714	\$ 17,400	\$ 17,303	\$ 23,247
Research progress payments.....	6,200	--	--	9,500	5,000	--	--
Contract manufacturing.....	6,617	7,299	9,960	9,113	4,458	2,451	1,140
Investment income.....	5,967	4,014	5,207	6,866	6,242	4,360	2,997
	45,827	26,624	39,706	45,193	33,100	24,114	27,384
Expenses:							
Research and development....	40,470	34,963	44,940	37,047	27,770	28,269	23,310
Loss in Amgen-Regeneron Partners.....	3,450	2,509	4,159	2,484	3,403	14,250	13,805
Contract manufacturing.....	6,828	3,452	3,612	5,002	2,617	1,115	72
Other.....	8,555	7,388	10,065	9,285	10,889	12,904	13,705
	59,303	48,312	62,776	53,818	44,679	56,538	50,892
Net loss.....	\$(13,476)	\$(21,688)	\$(23,070)	\$(8,625)	\$(11,579)	\$(32,424)	\$(23,508)
Weighted average number of Class A and common stock outstanding, basic and diluted.....							
	34,344	31,297	31,308	30,992	28,702	24,464	19,768
Net loss per share, basic and diluted.....	\$ (0.39)	\$ (0.69)	\$ (0.74)	\$ (0.28)	\$ (0.40)	\$ (1.33)	\$ (1.19)

AS OF SEPTEMBER 30, 2000

ACTUAL	AS ADJUSTED(1)
(IN THOUSANDS)	

BALANCE SHEET DATA:	
Cash, cash equivalents and marketable securities.....	\$158,499      \$298,924
Total assets.....	216,319      356,744
Stockholders' equity.....	190,972      331,397

(1) Gives effect to the sale of 4,000,000 shares of common stock in this offering, assuming a public offering price of \$37.125 per share, and our receipt of the net proceeds after deducting the underwriting discount and estimated offering expenses. See "Capitalization."

## RISK FACTORS

You should carefully consider the following risk factors before you decide to buy our common stock. If any of these risks actually occurs, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the trading price of our common stock to decline and you may lose part or all of your investment.

## RISKS RELATED TO OUR BUSINESS, INDUSTRY AND STRATEGY

## MOST DRUG RESEARCH AND DEVELOPMENT PROGRAMS FAIL.

Historically, the results from preclinical testing and early clinical trials often have not been predictive of results obtained in later large-scale clinical trials. Only a small minority of all research and development programs ultimately result in commercially successful drugs. It is not possible to predict whether any program will succeed until it actually produces a drug that is commercially marketed for a significant period of time. We are attempting to develop drugs for human therapeutic uses and we cannot assure you that any of our research and development activities will be successful or that any of our potential product candidates will be commercialized. If our clinical trials are not successful, we will not be able to develop and commercialize our product candidates.

Even if we are able to commence a Phase III study of AXOKINE, it is not possible to predict whether it will be successful in demonstrating adequate product safety and efficacy to support product approval. Weight loss observed in the recently completed Phase II study may not be predictive for the Phase III study. Factors such as duration of effects of the drug, antibodies against the drug, and compliance with self-injection over a prolonged period of time may negatively impact the outcome of the Phase III study. In addition, it is possible that as we test AXOKINE in a large and extended Phase III trial, side effects that were observed in the earlier clinical trials, as well as side effects that did not occur or went undetected in the completed smaller clinical studies, will become apparent, which will delay or prohibit the further development or commercialization of AXOKINE.

Amgen-Regeneron Partners is currently conducting Phase II clinical trials of NT-3 in patients with constipating conditions. The treatment of constipating conditions presents clinical trial risks in light of the complex and not wholly understood mechanisms of action that lead to the conditions, the concurrent use of other drugs to treat the underlying illnesses as well as the gastrointestinal condition, the potential difficulty of designing and achieving significant clinical endpoints, and other factors. No assurance can be given that the ongoing NT-3 clinical studies will be successful or that NT-3 will ever be commercialized.

In order to obtain regulatory approvals for the commercial sale of our product candidates, we will be required to complete extensive clinical trials in humans to demonstrate the safety and efficacy of the products. We have limited experience in conducting clinical trials. A clinical trial may fail for a number of reasons, including:

- failure to enroll a sufficient number of patients meeting eligibility criteria;
- failure of the product candidate to demonstrate safety or efficacy;
- the development of serious or life-threatening adverse events, for example, side effects, caused by or connected with exposure to the product candidate; and
- the failure of clinical investigators, trial monitors and other consultants, or trial subjects to comply with trial plan or protocol.

Any failure or substantial delay in successfully completing clinical trials and obtaining regulatory approval for our product candidates could severely harm our business.

## THERE ARE RISKS INVOLVED IN EXPANDING OUR INITIAL FOCUS AND BROADENING OUR PRODUCT PIPELINE.

Expanding from our initial focus on degenerative neurologic disease and broadening our product pipeline to include drug candidates for the treatment of other diseases involves risks. As we expand our

focus to broaden our product pipeline and as our scientific efforts lead us in new directions into conditions or diseases outside of our areas of experience and expertise, we will require additional internal expertise or external collaborations in areas in which we currently do not have substantial resources and personnel. As we develop drug candidates independently, we will require additional resources that may be difficult to obtain. We may have to enter into collaboration arrangements with others that may require us to relinquish rights to some of our technologies, product candidates, or products that we would otherwise pursue independently. We cannot assure you that we will be able to acquire the necessary expertise or enter into collaboration agreements on acceptable terms to develop additional drug candidates.

WE HAVE INCURRED SUBSTANTIAL LOSSES AND EXPECT TO INCUR LOSSES OVER THE NEXT SEVERAL YEARS.

We have not received revenue from the commercialization of our product candidates. We do not expect to receive any revenue from the commercialization of our product candidates for several years and we intend to continue to invest significantly in our product candidates. We have incurred losses in each year since inception of operations in 1988. As of September 30, 2000, we had an accumulated deficit of \$213.8 million. We do not know if we will ever have an approved product or achieve significant revenues or profitable operations. Even if we do successfully develop products that can be marketed and sold commercially, we will need to generate significant revenue from products to achieve and maintain profitability.

WE MAY REQUIRE ADDITIONAL FINANCING, WHICH MAY BE DIFFICULT TO OBTAIN AND MAY DILUTE YOUR OWNERSHIP INTEREST.

To date, we have received revenues from (1) our licensees and collaborators for research and development efforts, (2) Merck and Sumitomo Pharmaceuticals for contract manufacturing, and (3) investment income. We cannot assure you that these revenues will continue from our licensees or collaborators. In the absence of revenues from the commercialization of our product candidates or other sources, the amount, timing, nature, or source of which we cannot predict, our losses will continue as we conduct our research and development activities. Our activities may expand over time and may require additional resources and our operating losses may be substantial over at least the next several years. Our losses may fluctuate from quarter to quarter and will depend, among other factors, on the timing of certain expenses and on the progress of our research and development efforts.

In January 2001, Amgen-Regeneron Partners discontinued all clinical development of BDNF for the potential treatment of amyotrophic lateral sclerosis (ALS) following notification that BDNF did not provide a therapeutic advantage to ALS patients in clinical trials. BDNF is licensed to Sumitomo Pharmaceuticals Co., Ltd. for development in Japan. In light of the recent clinical trial results, it is likely that Sumitomo Pharmaceuticals will exercise its discretionary right to terminate the license for BDNF and we would not receive any further revenue from milestone payments, contract research and development, or contract manufacturing. In 2000, we recognized revenue from Sumitomo Pharmaceuticals of \$7.6 million, primarily related to contract manufacturing and a research progress payment.

We have had negative cash flow from operations in each year since our inception. We expect that the funding requirements for our activities will remain substantial and could increase significantly if, among other things, our development or clinical trial programs are successful or our research is expanded. For example, if we are able to commence a Phase III study of AXOKINE, the costs of conducting such a study, or any potential further studies required by the FDA or foreign regulatory authorities, would be significant. The Phase III study likely will involve the enrollment of several thousand patients with a treatment period of at least two years.

In addition, we are required to provide capital from time to time to fund and remain equal partners with Amgen in Amgen-Regeneron Partners. Our aggregate capital contributions to Amgen-Regeneron Partners from the partnership's inception in June 1993 through December 31, 2000 was \$55.2 million. We expect that our capital contributions for 2001 will total at least \$2.2 million. These contributions could increase or decrease, depending upon, among other things, the nature and cost of ongoing and additional

NT-3 studies that Amgen-Regeneron Partners may conduct, the outcomes of those studies and costs associated with the discontinuation of the BDNF studies.

The amount needed to fund our operations will also depend on other factors, including:

- the potential future need to expand our professional and support staff and facilities to support new areas of research and development;
- the success of our research and development programs;
- the status of patent and other intellectual property right developments; and
- the extent and success of any collaborative research arrangements.

We anticipate that the net proceeds from this offering, together with our cash, cash equivalents, and marketable securities of approximately \$154.4 million as of December 31, 2000, will be sufficient for our working capital needs for several years. However, we may need additional funding sooner due to a number of factors, including:

- the speed with which some of our earlier stage developmental products move into later stage clinical development;
- the identification of additional product candidates;
- the identification of new indications for a potential product in later stage clinical trials;
- the termination of any of our collaboration agreements;
- the acquisition of technologies or product candidates;
- the pursuit of new business opportunities;
- the cost of developing a marketing or sales force; and
- the cost of prosecuting or defending our patents and patent applications.

We have no established banking arrangements through which we can obtain short-term financing or a line of credit. We may seek additional funding through collaborative arrangements and public or private financing. Additional financing may not be available to us on acceptable terms or at all. If we are unable to obtain additional funding when needed, we may have to delay or scale back some of our programs or grant to third parties rights to development or other product rights. If we raise additional funds by issuing equity securities, further dilution to our then existing shareholders may result.

OUR SUCCESS DEPENDS UPON OBTAINING FDA AND FOREIGN REGULATORY APPROVAL TO CONDUCT CLINICAL TRIALS AND MARKET PRODUCT CANDIDATES CURRENTLY UNDER DEVELOPMENT.

The safety, effectiveness, testing, manufacture, distribution, labeling, storage, record-keeping, approval, advertising and promotion of our product candidates and the research and development activities associated with them are subject to extensive federal, state and foreign regulation. If we fail to obtain the necessary approvals or comply with regulatory requirements, or if any of our approvals are restricted, suspended or revoked, there could be a material adverse effect on us. Even if we are able to develop drugs and related therapies that are approved for sale by the FDA or by foreign regulatory authorities, we cannot assure you that any such drugs or related therapies will be commercially successful. None of our product candidates have been approved for sale in the United States or any foreign market.

The compounds we are developing will require significant additional time-consuming and costly research and development, including further preclinical and clinical testing, before we can file an application for commercial approval. As an initial step in the FDA regulatory approval process, preclinical studies are typically conducted in animals to identify potential safety problems. The results of preclinical studies are submitted to the FDA as a part of the Investigational New Drug Application, or the IND, which is filed to comply with FDA regulations before beginning human clinical studies.

The submission of an IND may not result in FDA authorization to commence clinical trials. Similarly, once we have completed early stage clinical testing of a product candidate, there is no assurance that we will be able to commence larger scale clinical trials. For example, before we are able to commence Phase III testing of AXOKINE, we will need to meet with the FDA and review the results of our prior clinical and preclinical studies. During the Phase I study of AXOKINE that was conducted in 1999, we observed in higher single doses, incidents of nausea, vomiting, and herpes simplex virus, or HSV. HSV was also reported in previous clinical studies of CNTF, AXOKINE's parent molecule. In addition, in the Phase I study, one patient in the multiple low dose (a dose of 1.0 mcg/kg/day) group, who was HSV positive prior to treatment and had been previously diagnosed with Bell's palsy, had a recurrence of Bell's palsy approximately two weeks after the patient's last administration of AXOKINE. In the recently completed Phase II study of AXOKINE, reported side effects included nausea, cough, and vomiting. In the Phase II study, there was no increase compared to placebo in the incidence of HSV in patients taking AXOKINE.

It is possible that as we test AXOKINE in a large and extended Phase III trial, these side effects as well as side effects that did not occur or went undetected in smaller clinical trials will become apparent. Furthermore, no assurances can be given that the FDA will permit us to commence large-scale, Phase III testing of AXOKINE without first undertaking additional clinical or preclinical studies. This additional testing could substantially delay, or restrict, the further development of AXOKINE.

We may not complete testing of any of our product candidates within any specific time period, if at all. Our compounds may prove to have undesirable and unintended side effects that may interrupt or delay clinical studies and could ultimately prevent or limit their commercial use. The creation of antibodies against the therapeutic protein may totally or partially neutralize the effectiveness of the protein or, in some cases, the antibodies may cross-react with the patient's own proteins, resulting in an "auto-immune type" disease. We or the regulatory authorities may suspend or terminate clinical trials at any time if the people participating in such trials are believed to be exposed to unacceptable health risks.

Clinical trials, if completed, may not show any potential product to be safe or effective. Thus, the FDA and other regulatory authorities may not approve any of our product candidates for any disease indication.

The extensive regulatory approval process required by the FDA and by comparable agencies in other countries can take many years and requires the expenditure of substantial resources. This gives larger companies with greater financial resources a competitive advantage. Data obtained from preclinical and clinical activities are subject to different interpretations, which could delay, limit or prevent FDA regulatory approval. We may encounter delays or rejections based upon changes in FDA policy for drug approval during the period of development and FDA regulatory review. We may also encounter similar delays or rejection of applications in foreign countries. We cannot assure you that even after such time and expenditures, regulatory approval will be obtained for any compounds we develop. Moreover, even if approval is granted, such approval may have limitations on the indicated uses for which compounds may be marketed. Subsequent discovery of previously unknown problems with a product or its manufacture may result in restrictions on the product or manufacturer, including withdrawal of the product from the market.

WE FACE SUBSTANTIAL COMPETITION, WHICH MAY RESULT IN OTHERS DISCOVERING, DEVELOPING OR COMMERCIALIZING PRODUCTS BEFORE OR MORE SUCCESSFULLY THAN WE DO.

There is substantial competition in the biotechnology and pharmaceutical industries from pharmaceutical, biotechnology, and chemical companies. Many of our competitors have substantially greater research, preclinical, and clinical product development and manufacturing capabilities, and financial, marketing and human resources than we do. Our smaller competitors may also be significant if they acquire or discover patentable inventions, form collaborative arrangements, or merge with large pharmaceutical companies. We cannot assure you that we will be able to produce approved compounds that have commercial potential. Even if we achieve product commercialization, one or more of our competitors may achieve product

commercialization earlier than we do or obtain patent protection that dominates or adversely affects our activities.

There is substantial competition in the discovery and development of treatments for obesity, as well as established and cost-effective and emerging prescription and over-the-counter treatments for this condition. For example, Hoffmann-LaRoche, Inc. and Knoll Pharmaceuticals already market well-established drugs for the treatment of obesity and Amgen and a number of other pharmaceutical companies are developing leptin and related molecules. Clinical trials of leptin are under way. Some of these drugs may offer competitive advantages over AXOKINE. For example, AXOKINE currently is available only in injectible form, while the currently available marketed drugs for the treatment of obesity are delivered in oral dosage forms, which generally are favored by patients over injectible drugs. Therefore, even if AXOKINE is approved for sale, the fact that it must be delivered by injection may severely limit its market acceptance among patients and physicians.

Similarly, marketed products for the treatment of rheumatoid arthritis and asthma are available as either oral or inhaled drugs, whereas our Cytokine Traps currently are only planned for clinical trials as injectibles. The markets for both rheumatoid arthritis and asthma are very competitive. Several new, highly successful drug candidates recently became available for these disease states. Examples include the TNF-antagonists Enbrel(R) and Remicade(R) for rheumatoid arthritis and the leukotriene-modifier Singulair(R), as well as various inexpensive corticosteroid drugs for asthma.

Many companies are developing drugs designed to block the actions of VEGF specifically and angiogenesis in general. A variety of approaches have been employed, including antibodies to VEGF, antibodies to the VEGF receptor, small molecule antagonists to the VEGF receptor tyrosine kinase, as well as multiple other anti-angiogenesis strategies. Many of these alternative approaches may offer competitive advantages to our VEGF Trap, in efficacy, side-effect profile, or form of delivery. Additionally, many of these developmental drugs may be at a more advanced stage of development than our product candidate.

Many firms and entities are engaged in research and development in the areas of cytokines, interleukins, angiogenesis, and muscle conditions. Some of these competitors are currently conducting advanced preclinical and clinical research programs in these areas. These and other competitors may have established substantial intellectual property and other competitive advantages.

The treatment of constipating conditions is highly competitive, with a number of companies providing over-the-counter remedies and other competitors attempting to discover and develop improved over-the-counter or prescription treatments. In addition, many pharmaceutical and biotechnology companies are attempting to discover and develop small-molecule based therapeutics, similar in at least certain respects to our program with Procter & Gamble. In these and related areas, intellectual property rights have been sought and certain rights have been granted to competitors and potential competitors of ours and we may be at a substantial competitive disadvantage in such areas as a result of, among other things, our lack of experience, trained personnel, and expertise. A number of corporate and academic competitors are involved in the discovery and development of novel therapeutics using tyrosine kinase receptors, orphan receptors, and compounds that are the focus of other research or development programs we are now conducting. These competitors include Amgen and Genentech, as well as many others.

If a competitor announces a successful clinical study involving a product that may be competitive with one of our product candidates or an approval by a regulatory agency of the marketing of a competitive product, such announcement may have a material adverse effect on our operations, or future prospects, or the price of our common stock.

We also compete with academic institutions, governmental agencies, and other public or private research organizations, which conduct research, seek patent protection, and establish collaborative arrangements for the development and marketing of products that would provide royalties for use of their technology. These institutions are becoming more active in seeking patent protection and licensing arrangements to collect royalties for use of the technology that they have developed. Products developed in

this manner may compete directly with products we develop. We also compete with others in acquiring technology from such institutions, agencies, and organizations.

Our ability to compete will depend on how fast we can develop safe and effective product candidates, complete clinical testing and approval processes and supply commercial quantities of the product to the market. Competition among product candidates approved for sale will also be based on efficacy, safety, reliability, availability, price, patent position, and other factors.

WE DEPEND ON THE COLLABORATIVE EFFORTS OF OUR ACADEMIC AND CORPORATE PARTNERS FOR RESEARCH, DEVELOPMENT AND COMMERCIALIZATION OF SOME OF OUR PRODUCT CANDIDATES.

Our strategy for research, development and commercialization of some of our products involves entering into various arrangements with academic and corporate partners and others. As a result, our strategy depends, in part, upon the success of these outside parties in performing their responsibilities. Our collaborators may also be our competitors, such as Amgen. We cannot control the amount and timing of resources that our collaborators devote to performing their contractual obligations. We cannot assure you that these parties will perform their obligations as expected or that any revenue will be derived from these arrangements.

If any of our collaborators breaches or terminates its agreement with us or otherwise fails to conduct its collaborative activities in a timely manner, the development or commercialization of the product candidate or research program under such collaborative arrangement may be delayed. If that is the case, we may be required to undertake unforeseen additional responsibilities or to devote unforeseen additional funds or other resources to such development or commercialization, or such development or commercialization could be terminated.

In August 2000, we and Procter & Gamble agreed through a binding memorandum of understanding to enter into a new long-term collaboration agreement, replacing the companies' 1997 agreement. The new agreement will focus the companies' collaborative research on therapeutic areas that are of particular interest to Procter & Gamble. Under the original 1997 collaboration agreement, research support from Procter & Gamble would have been \$6.8 million per quarter (before adjustments for future inflation) for the period from July 2000 through June 2002. Under the new agreement, beginning in the first quarter of 2001, research support from Procter & Gamble will be \$2.5 million per quarter (before adjustments for future inflation) through December 2005. We and Procter & Gamble have divided rights to the programs that are no longer part of the companies' collaboration, and we are developing those programs where we have retained rights, including the VEGF Trap, the Angiopoietins and the Regeneron Orphan Receptors (RORs), at our own expense.

The termination or cancellation of collaborative arrangements could adversely affect our financial condition, intellectual property position and operations. In addition, our collaboration agreement with Procter & Gamble has an "opt-out" provision whereby a party may decline to participate further in a research or product development program. In such cases, the opting-out party will generally not have any further funding obligation and will not have any rights to the product or program in question (but may be entitled to a royalty on any product sales). If Procter & Gamble were to opt out of a product development program, and we were not to find a new partner, we would bear the full cost of the program. This could lead to delays in the research, development or commercialization of the affected products and could adversely affect our financial condition, intellectual property position and operations. In addition, disagreements between collaborators and us could lead to delays in the collaborative research, development, or commercialization of certain products or could require or result in formal legal process or arbitration for resolution. These consequences could be time-consuming and expensive and could have material adverse effects on us.

Other than our contractual rights under our license agreements, we may be limited in our ability to convince our licensees to fulfill their obligations. If our licensees fail to act promptly and effectively, or if a dispute arises, it could have a material adverse effect on our results of operations and the price of our common stock.

We rely upon scientific, technical and clinical data supplied by academic and corporate collaborators, licensors, licensees, independent contractors and others in the evaluation and development of potential therapeutic compounds. We cannot assure you that there are no errors or omissions in this data that would materially adversely affect the development of these compounds.

We may seek additional collaborative arrangements to develop and commercialize our products in the future. We cannot assure you that we will be able to negotiate acceptable collaborative arrangements in the future or that they will be on favorable terms or that any collaborative arrangements will be successful. In addition, our collaborative partners may pursue alternative technologies or develop alternative compounds independently or in collaboration with others as a means of developing treatments for the diseases targeted by their collaborative programs with us.

#### THERE ARE RISKS RELATING TO PRODUCT MANUFACTURING.

Our ability to conduct timely preclinical and clinical research and development programs, obtain regulatory approval, commercialize our product candidates and fulfill our contract manufacturing obligations to others will depend, in part, upon our ability to manufacture our products, either directly or through third parties, in accordance with FDA and other regulatory requirements.

If we are unable to manufacture our product candidates, we would be unable to proceed with or could experience delays in the regulatory process for our product candidates under development, and experience delays in the commercialization of our product candidates. We cannot assure you that we will be able to manufacture products successfully or in a cost-effective manner at our facilities. We may also have difficulties obtaining the raw materials and supplies necessary to manufacture our product candidates or the products we manufacture for others. If we are unable to develop our own manufacturing facilities or to obtain or retain third-party manufacturing on acceptable terms, we may not be able to conduct certain future preclinical and clinical testing or to supply commercial quantities of our product candidates. Our dependence upon third parties for the manufacture of some of our products and related therapies may adversely affect our profit margins and our ability to develop and deliver products on a timely and competitive basis. For example, we are aware of only one supplier of the reagent necessary to produce a pegylated formulation of AXOKINE, which is substantially longer acting than unmodified AXOKINE in preclinical studies. Any problems with the supply of reagent from this vendor could result in the delay or interruption in the development of any pegylated form of AXOKINE.

In addition, if our manufacturing facilities fail to comply with FDA and other regulatory requirements, we will be required to suspend manufacturing. This will have a material adverse effect on our financial condition, results of operations and cash flow.

#### SINCE WE HAVE NO SALES AND MARKETING EXPERIENCE OR INFRASTRUCTURE, WE MAY HAVE TO RELY ON THIRD PARTIES.

We have no sales, marketing and distribution experience or infrastructure. We may have to rely significantly on sales, marketing and distribution arrangements with third parties for the products we are developing. If we choose to depend on third parties for the marketing and sale of our product candidates, should any be approved for sale, the cost of using such third parties may adversely affect our profit margins. If in the future we determine to perform sales, marketing and distribution functions ourselves, we would face a number of additional risks, including:

- we may not be able to attract and build a significant marketing or sales force;
- the significant cost of establishing a marketing or sales force may not be justifiable in light of any product revenues; and
- our direct sales and marketing efforts may not be successful.

#### OUR PRODUCT CANDIDATES MAY NOT ACHIEVE COMMERCIAL SUCCESS.

Even if clinical trials demonstrate safety and efficacy of our product candidates and the necessary regulatory approvals are obtained, the commercial success of any of our product candidates will depend upon their acceptance by patients, the medical community and third-party payors and on our ability to

successfully develop, manufacture and market our product candidates. Among the factors that we believe will materially affect acceptance of our product candidates are:

- the timing of receipt of approvals for marketing our products and the countries in which those approvals are obtained;
- the safety and efficacy of our product candidates;
- the success of physician education programs;
- the willingness of physicians and patients to accept injectible dosage forms;
- the cost of our products in comparison with conventional or alternative therapeutic products; and
- the availability of government and third-party payor reimbursement of our products.

Our product candidates, if successfully developed, will compete with a number of drugs and therapies manufactured and marketed by major pharmaceutical and biotechnology companies. Physicians, patients, and the medical community may not accept and utilize any product candidates that we develop. If our products do not achieve significant market acceptance, we will not be able to recover the significant investment we have made in developing such products and our business would be severely harmed.

IF WE FAIL TO OBTAIN AN ADEQUATE LEVEL OF REIMBURSEMENT FOR OUR FUTURE PRODUCTS BY THIRD-PARTY PAYORS, THERE MAY BE NO COMMERCIALY VIABLE MARKETS FOR OUR PRODUCTS.

The success of our products will depend, in part, upon the extent to which a consumer will be willing to pay the price or be able to obtain reimbursement for the cost of these products from government health administration authorities, private health insurers and other organizations.

Significant uncertainties exist as to the reimbursement status of newly approved therapeutic products. Medicare generally does not provide reimbursement for self-administered prescription therapeutic agents. We cannot assure you that (1) reimbursement in the United States or foreign countries will be available for any of our products, or (2) if reimbursement is available, there will be no decrease in the future or (3) reimbursement amounts will not reduce the demand for or the price of our products. The unavailability or inadequacy of third-party reimbursement for our products could have a material adverse effect on us.

Third-party payors are increasingly challenging the prices charged for medical services and products. Moreover, the trend towards managed care in the United States and the growth of organizations such as health maintenance organizations, which could control or significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care or reduce government insurance programs, may result in lower prices for our products. The cost containment measures that health care providers are instituting and the effect of any health care reform could affect our ability to sell our products and may have a material adverse effect on us. We are unable to forecast what additional legislation or regulation, if any, relating to the health care industry or third-party coverage and reimbursement may be enacted in the future or what effect such legislation or regulation would have on our business.

RECRUITING AND RETAINING QUALIFIED SCIENTIFIC AND MANAGEMENT PERSONNEL TO PERFORM RESEARCH AND DEVELOPMENT WORK AND TO COMMERCIALIZE PRODUCTS ARE CRITICAL TO OUR SUCCESS.

Although we believe we have been successful in attracting and retaining skilled and experienced scientific and management personnel, we cannot assure you that we will be able to continue to attract and retain such personnel on acceptable terms. The loss of any of our key personnel, in particular (1) our Chairman, P. Roy Vagelos, M.D., (2) our President and Chief Executive Officer, Leonard S. Schleifer, M.D., Ph.D. and (3) our Chief Scientific Officer, George D. Yancopoulos, M.D., Ph.D., may have an adverse effect on us. In addition, our anticipated growth and expansion into new areas requiring additional expertise are expected to place increased demands on our resources and require the recruitment of

additional management personnel and the development of additional expertise by existing management personnel. Attracting and retaining qualified personnel will be critical to our success. Many of our competitors are established pharmaceutical and biotechnology companies that may have greater success in recruiting skilled scientific workers from the limited pool of available talent. The failure to attract and retain key management and scientific personnel could have a material adverse effect on us.

WE COULD BE EXPOSED TO SIGNIFICANT LIABILITY CLAIMS AND OUR INSURANCE COVERAGE MAY NOT BE ADEQUATE TO COVER THESE CLAIMS.

The testing, manufacturing, and marketing of human pharmaceutical products entail significant inherent risks. Their use in clinical trials and their sale may expose us to liability claims. These claims might be made directly by patients, consumers, pharmaceutical companies, or others selling the products. We are insured by health care product liability insurance policies, including a policy carried by Amgen-Regeneron Partners, the purpose of which is to cover certain claims that could arise during the clinical trials of AXOKINE, the IL-1 Trap, and NT-3. Such coverage or the amount and scope of any coverage obtained in the future may be inadequate to protect our company in the event of a successful liability claim and we cannot assure you that the amount of such insurance can be purchased, increased or renewed. We cannot assure you that we will avoid a significant product liability claim or recall that could have a material adverse effect on us.

RISKS RELATED TO INTELLECTUAL PROPERTY

WE MAY NOT BE ABLE TO OBTAIN PATENT PROTECTION FOR OUR DISCOVERIES AND WE MAY INFRINGE PATENT RIGHTS OF OTHERS.

We believe that patent protection of, and freedom to use, products or processes that may result from our research and development efforts, or may be developed by our licensors, licensees or collaborators are important to the possible commercialization of our product candidates. We or our licensors or collaborators have filed patent applications on products and processes relating to AXOKINE, Cytokine Traps, Angiopoietins, and NT-3, as well as other technologies and inventions in the United States and in certain foreign countries. Although we have obtained a number of U.S. patents, we cannot assure you that any additional patents will be issued. Moreover, we cannot assure you that our products or processes will not be found to infringe the patents of others or that any of our issued patents will provide adequate protection against competitive products or otherwise be commercially valuable.

In September 2000, Immunex Corporation filed a request with the European Patent Office seeking the declaration of an Opposition regarding our European patent relating to Cytokine Traps. This is a legal challenge to the validity and scope of our patent. Although we plan to defend the patent diligently, we cannot predict whether the scope of the patent will be affected in the future should an Opposition be declared.

In addition, patent law relating to the patentability and scope of claims in the biotechnology field is evolving and our patent rights are subject to this additional uncertainty. Others may independently develop similar products or processes to those developed by us, duplicate any of our products or processes or, if patents are issued to us, design around any products and processes covered by our patents. We expect to continue to file product and process patent applications with respect to our inventions. However, we cannot assure you that we will file any such applications or, if filed, that the patents will be issued. Patents issued to or licensed by us may be infringed by the products or processes of others.

Defense and enforcement of our rights can be expensive and time consuming, even if the outcome is favorable to us. It is possible that patents issued to or licensed to us will be successfully challenged, that a court may find that we are infringing validly issued patents of third parties, or that we may have to alter our products or processes or pay licensing fees or cease certain activities to take into account patent rights of third parties, causing additional unexpected costs and delays which may have a material adverse effect on us.

IF WE ARE NOT ABLE TO KEEP OUR TRADE SECRETS CONFIDENTIAL, OUR TECHNOLOGY AND INFORMATION MAY BE USED BY OTHERS TO COMPETE AGAINST US.

In addition to our reliance on patents, we attempt to protect our proprietary products and processes by relying on trade secret laws and nondisclosure and confidentiality agreements and exclusive licensing arrangements with our employees and certain other persons who have access to our proprietary products or processes or have licensing or research arrangements exclusive to us. Despite these protections, no assurance can be given that these agreements or arrangements will provide meaningful protection for our trade secrets in the event of unauthorized use or disclosure of such information or that others will not independently develop or obtain access to such products or processes or that our competitive position will not be adversely affected thereby. No assurance can be given that others will not independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or technology or that we can meaningfully protect our rights to our trade secrets.

WE MAY BECOME INVOLVED IN EXPENSIVE PATENT LITIGATION OR OTHER INTELLECTUAL PROPERTY PROCEEDINGS WHICH COULD RESULT IN LIABILITY FOR DAMAGES OR STOP OUR PRODUCT DEVELOPMENT AND COMMERCIALIZATION EFFORTS.

There has been substantial litigation and other proceedings regarding intellectual property rights in the pharmaceutical and biotechnology industries. We may become a party to patent litigation or other proceedings regarding intellectual property rights. In September 2000, Immunex Corporation filed a request with the European Patent Office seeking the declaration of an Opposition regarding the scope of our European patent relating to Cytokine Traps. This is a legal challenge to the validity and scope of our patent. Although we plan to defend the patent diligently, we cannot predict whether the scope of the patent will be affected in the future should an Opposition be declared.

Other types of situations in which we may become involved in patent litigation or other intellectual property proceedings include:

- we may initiate litigation or other proceedings against third parties to enforce our patent rights;
- we may initiate litigation or other proceedings against third parties to seek to invalidate the patents held by these third parties or to obtain a judgment that our products or services do not infringe the third parties' patents;
- if our competitors file patent applications that claim technology also claimed by us, we may participate in interference or opposition proceedings to determine the priority of invention; and
- if third parties initiate litigation claiming that our processes or products infringe their patent or other intellectual property rights, we will need to defend against such claims.

The cost to us of any patent litigation or other proceedings, even if resolved in our favor, could be substantial. Some of our competitors may be able to sustain the cost of such litigation or proceedings more effectively than we can because of their substantially greater financial resources. If a patent litigation or other intellectual property proceeding is resolved unfavorably to us, we may be enjoined from manufacturing or selling our products and services without a license from the other party and be held liable for significant damages. We may not be able to obtain any required license on commercially acceptable terms, if at all.

Uncertainties resulting from the litigation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace. Patent litigation and other proceedings may also absorb significant management time.

IF WE BREACH ANY OF THE AGREEMENTS UNDER WHICH WE LICENSE TECHNOLOGY FROM OTHERS, WE COULD LOSE LICENSE RIGHTS THAT ARE IMPORTANT TO OUR BUSINESS.

We are a party to technology licenses that are important to our business and expect to enter into additional licenses in the future. These licenses impose commercialization, sublicensing, royalty, insurance

and other obligations on us. If we fail to comply with these requirements, our licensors may have the right to terminate our licenses. Such termination may have a negative impact on our business.

#### RISKS RELATING TO OUR COMMON STOCK

##### OUR STOCK PRICE COULD BE VOLATILE, WHICH COULD CAUSE YOU TO LOSE PART OR ALL OF YOUR INVESTMENT.

There has been a history of significant volatility in the market price of shares of biotechnology companies, including our shares, and it is likely that the market price of our common stock will continue to be highly volatile. In 1998, the bid price for our common stock fluctuated from a low of \$5.75 a share to a high of \$11.00 a share. In 1999, the bid price fluctuated from a low of \$5.38 per share to a high of \$13.00 per share. From January 1, 2000 to January 24, 2001, the bid price fluctuated from a low of \$11.50 per share to a high of \$56.44 per share. The following factors may have a significant effect on the market price of our common stock:

- fluctuations in our operating results;
- clinical trial results;
- announcements of technological innovations or new commercial therapeutic products introduced by us or our competitors;
- governmental regulation;
- regulatory delays;
- litigation;
- developments in patent or other proprietary rights;
- public concern as to the safety or other implications of the drugs sought to be developed by us or the genetic engineering involved in their production; and
- general market conditions.

Any clinical trial results that are below the expectations of financial analysts or investors would most likely cause our stock price to drop dramatically. Similarly, our stock is likely to drop dramatically if we are not permitted by the FDA to commence a Phase III trial for AXOKINE in 2001 or if the Phase II NT-3 trials expected to be completed in mid-2001 fail to achieve their expected results.

##### OUR EXISTING SHAREHOLDERS MAY BE ABLE TO INFLUENCE THE OUTCOME OF CORPORATE ACTIONS.

Holders of Class A stock, who are the shareholders who purchased their stock from us before our initial public offering, are entitled to ten votes per share and holders of common stock are entitled to one vote per share. Upon completion of this offering, holders of Class A stock will hold 6.4% of the total of our outstanding shares of common stock and Class A stock, or collectively, our common shares, and have 40.6% of the combined voting power of the common shares and, if acting together, will be in position to significantly influence the election of our directors and to effect or prevent certain corporate transactions which require majority or supermajority approval of the combined classes, including mergers and other business combinations. Specifically, upon the completion of this offering:

- our current officers and directors will own 9.5% of our outstanding common shares and 38.7% of the combined voting power of our common shares;
- Procter & Gamble will hold 16.3% of our outstanding common shares and 10.4% of the combined voting power of our common shares; and
- Amgen will hold 12.0% of our outstanding common shares and 7.6% of the combined voting power of our common shares.

WE HAVE ANTITAKEOVER DEFENSES THAT COULD DELAY OR PREVENT AN ACQUISITION AND COULD ADVERSELY AFFECT THE PRICE OF OUR COMMON STOCK.

New York corporate law and our amended and restated certificate of incorporation and by-laws contain provisions that could have the effect of delaying or preventing a change in control of our company or our management that shareholders may consider favorable or beneficial. These provisions could discourage proxy contests and make it more difficult for you and other shareholders to elect directors and take other corporate actions. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock. These provisions include:

- authorization to issue "blank check" preferred stock, which is preferred stock that can be created and issued by the board of directors without prior shareholder approval, with rights senior to our common stockholders; and
- a staggered board of directors, so that it would take three successive annual meetings to replace all directors.

In addition, we have a shareholders rights plan which will make it more difficult for a third party to acquire us without the support of our board of directors and principal shareholders.

A SIGNIFICANT NUMBER OF OUR SHARES ARE ELIGIBLE FOR RESALE. THIS COULD REDUCE OUR SHARE PRICE AND IMPAIR OUR ABILITY TO RAISE FUNDS IN NEW SHARE OFFERINGS.

Procter & Gamble and Amgen own 18.1% (or 6,662,505 shares) and 13.4% (or 4,916,808 shares), respectively, of our outstanding common shares. Our agreements with each of Procter & Gamble and Amgen grant them demand and piggyback registration rights with respect to their shares of common stock. Either one of these companies could cause a significant number of shares of our common stock to be registered and sold in the public market, particularly in light of the discontinuation of certain of our collaborative efforts with Procter & Gamble and Amgen, which could cause our stock price to decline.

Immediately after completion of this offering, we will have 40,828,153 common shares outstanding and available for resale beginning at various points of time in the future. In addition, we will have 7,520,327 outstanding stock options held by our directors, officers, and employees and 107,400 warrants held by Medtronic as of January 23, 2001. Sales of substantial amounts of shares of our common stock in the public market after this offering, or the perception that those sales will occur, could cause the market price of our common stock to decline. Those sales also might make it more difficult for us to sell equity and equity-related securities in the future at a time and at a price that we consider appropriate.

YOU WILL SUFFER IMMEDIATE AND SUBSTANTIAL DILUTION.

The price you will pay for our common stock in this offering will be substantially higher than the \$8.13 pro forma net tangible book value per share of our outstanding common shares as of September 30, 2000. As a result, at an assumed offering price of \$37.125, you will experience immediate dilution of \$29.00 in net tangible book value per share, and our current shareholders will experience an immediate increase in the net tangible book value per share of their common shares of \$2.93.

## FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference include forward-looking statements. We have based these forward-looking statements on our current expectations and projections about future events. These forward-looking statements include, among other things, statements relating to:

- our anticipated business strategies;
- our anticipated clinical trials;
- our intention to introduce new products candidates;
- our relationships with collaborators;
- anticipated trends in our businesses;
- future capital expenditures; and
- our ability to conduct clinical trials and obtain regulatory approval.

The forward-looking statements included in this prospectus or in the documents incorporated by reference are subject to risks, uncertainties and assumptions about us. Our actual results of operations may differ materially from the forward-looking statements as a result of, among other things, the success or failure of our clinical trials, the speed at which our clinical trials progress, the success of our competitors in developing products equal or superior to ours, the success of our collaborative relationships and the other reasons described under "Risk Factors." We undertake no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events or otherwise. In light of these risks, uncertainties and assumptions, the forward-looking events discussed in this prospectus might not occur.

For these statements, we claim the protection of the safe harbor for forward-looking statements contained in Section 21E of the Securities Act.

## USE OF PROCEEDS

We will receive approximately \$140.4 million of net proceeds from the sale of 4,000,000 shares of our common stock, based on the public offering price of \$37.125 per share, after deducting underwriting discounts and commissions and the estimated expenses of this offering. If the underwriters' over-allotment option is exercised in full, we estimate that such net proceeds will be approximately \$161.6 million.

We intend to use the net proceeds for research and development, commercialization expenses, capital expenditures, potential acquisitions, working capital, and other general corporate purposes, including:

- all of the costs to fund preclinical and clinical development of product candidates that are being developed independent of any corporate partner, currently including AXOKINE, Pegylated AXOKINE, IL-1 Trap, IL-4/IL-13 Trap, VEGF Trap, and the Angiopoietins;
- our share of the costs to fund preclinical and clinical development of product candidates that have been partnered;
- basic research, including collaborative research in therapeutic areas that have been partnered;
- continued development of novel technology platforms, including potential efforts to commercialize these technologies;
- expenses for commercialization of our product candidates;
- purchase of equipment and expansion of, or construction of additional, research and development laboratories and manufacturing facilities; and
- potential acquisitions of companies and technologies which complement our business.

Pending application of the net proceeds as described above, we intend to invest the net proceeds of this offering primarily in U.S. Government and other investment grade obligations, interest bearing money market funds and other financial instruments. See "Investment Company Act Considerations."

## DIVIDEND POLICY

We have never paid cash dividends and do not anticipate paying any in the foreseeable future. In addition, under the terms of certain of our debt agreements, we are not permitted to declare or pay cash dividends.

## CAPITALIZATION

The following table sets forth our capitalization as of September 30, 2000 and as adjusted to give effect to our sale of 4,000,000 shares of our common stock in this offering, at an assumed offering price of \$37.125, after deducting underwriting discounts and commissions and estimated expenses of this offering, and the application of the estimated net proceeds. See "Use of Proceeds."

	AT SEPTEMBER 30, 2000	
	ACTUAL	AS ADJUSTED
	(IN THOUSANDS, EXCEPT SHARE DATA)	
Cash, cash equivalents and marketable securities.....	\$ 158,499	\$ 298,924
Capital lease obligations -- long-term portion.....	\$ 694	\$ 694
Note payable -- long-term portion.....	1,483	1,483
Stockholders' equity:		
Preferred stock, \$.01 par value; 30,000,000 shares authorized; issued and outstanding -- none.....	--	--
Class A stock, \$.001 par value, convertible into common stock; 40,000,000 shares authorized, 2,759,095 shares issued and outstanding -- actual and as adjusted.....	3	3
Common stock, \$.001 par value; 60,000,000 shares authorized; 33,995,109 shares issued and outstanding -- actual; 37,995,109 shares issued and outstanding -- as adjusted.....	34	38
Additional paid-in capital.....	404,916	545,337
Accumulated deficit.....	(213,779)	(213,779)
Accumulated other comprehensive loss.....	(202)	(202)
Total stockholders' equity.....	190,972	331,397
Total capitalization.....	\$ 193,149	\$ 333,574

As of December 31, 2000, cash, cash equivalents and marketable securities totaled approximately \$154.4 million.

## DILUTION

As of September 30, 2000, our net tangible book value before the offering was \$191.0 million or \$5.20 per common share. "Net tangible book value per share" is determined by dividing our net tangible book value (total assets less total liabilities) by the number of common shares outstanding. After giving effect to the sale of the shares of our common stock in this offering at an assumed offering price of \$37.125 and after deducting underwriting discounts and commissions and the estimated expenses of this offering, our pro forma net tangible book value as of September 30, 2000 would have been \$331.4 million in the aggregate, or \$8.13 per common share. This represents an immediate increase in net tangible book value of \$2.93 per common share to existing holders and immediate dilution of \$29.00 per common share to new investors purchasing shares of common stock in this offering. The following table illustrates this per share dilution:

Assumed public offering price.....		\$37.13
Net tangible book value per common share before this offering.....	\$5.20	
Increase attributable to new investors.....	2.93	
	-----	
Pro forma net tangible book value per common share after this offering.....		8.13
		-----
Dilution per common share to new investors.....		\$29.00
		=====

"Dilution per common share to new investors" means the difference between the public offering price per share of common stock and the pro forma net tangible book value per common share after giving effect to this offering.

## SELECTED FINANCIAL DATA

We have derived the selected financial data presented below for the years ended December 31, 1999, 1998 and 1997 and at December 31, 1999 and 1998 from our audited financial statements and notes thereto included in our Annual Report on Form 10-K for the year ended December 31, 1999 which is incorporated by reference in this prospectus. We have derived the selected financial data for the years ended December 31, 1996 and 1995 and at December 31, 1997, 1996 and 1995 from our audited financial statements and notes thereto not included in this prospectus. We have derived the selected financial data for the nine month periods ended September 30, 2000 and 1999 from unaudited financial statements included in our September 2000 Form 10-Q which, in the opinion of our management, include all adjustments (consisting only of normal recurring adjustments) that are necessary for a fair presentation of results of operations for such periods. You should read the selected financial data together with the audited and unaudited financial statements and the section entitled "Management's Discussion and Analysis of Financial Condition and Results of Operations" in our Annual Report on Form 10-K for the year ended December 31, 1999 and our quarterly report on Form 10-Q for the quarter ended September 30, 2000 which is incorporated by reference in this prospectus.

	NINE MONTHS ENDED SEPTEMBER 30,		YEAR ENDED DECEMBER 31,				
	2000	1999	1999	1998	1997	1996	1995
(IN THOUSANDS, EXCEPT PER SHARE DATA)							
<b>STATEMENT OF OPERATIONS DATA:</b>							
<b>Revenues:</b>							
Contract research and development.....	\$ 27,043	\$ 15,311	\$ 24,539	\$19,714	\$ 17,400	\$ 17,303	\$ 23,247
Research progress payments.....	6,200	--	--	9,500	5,000	--	--
Contract manufacturing.....	6,617	7,299	9,960	9,113	4,458	2,451	1,140
Investment income.....	5,967	4,014	5,207	6,866	6,242	4,360	2,997
	45,827	26,624	39,706	45,193	33,100	24,114	27,384
<b>Expenses:</b>							
Research and development.....	40,470	34,963	44,940	37,047	27,770	28,269	23,310
Loss in Amgen-Regeneron Partners.....	3,450	2,509	4,159	2,484	3,403	14,250	13,805
General and administrative.....	5,203	4,691	6,355	5,838	5,765	5,880	5,764
Depreciation and amortization.....	3,125	2,452	3,426	3,019	4,389	6,084	5,886
Contract manufacturing.....	6,828	3,452	3,612	5,002	2,617	1,115	72
Interest.....	227	245	284	428	735	940	1,205
Other.....	--	--	--	--	--	--	850
	59,303	48,312	62,776	53,818	44,679	56,538	50,892
Net loss.....	\$(13,476)	\$(21,688)	\$(23,070)	\$(8,625)	\$(11,579)	\$(32,424)	\$(23,508)
<b>Weighted average number of Class A and common stock outstanding, basic and diluted.....</b>							
	34,344	31,297	31,308	30,992	28,702	24,464	19,768
Net loss per share, basic and diluted.....	\$ (0.39)	\$ (0.69)	\$ (0.74)	\$ (0.28)	\$ (0.40)	\$ (1.33)	\$ (1.19)

	AT SEPTEMBER 30,		AT DECEMBER 31,				
	2000	1999	1999	1998	1997	1996	1995
(IN THOUSANDS)							
<b>BALANCE SHEET DATA:</b>							
Cash, cash equivalents and marketable securities.....	\$158,499	\$ 87,433	\$ 93,599	\$113,530	\$128,041	\$ 97,028	\$59,622
Total assets.....	216,319	134,380	136,999	156,915	168,380	137,582	93,811
Capital lease obligations and note payable, long-term portion.....	2,177	2,150	2,731	3,066	3,752	5,148	5,978
Stockholders' equity.....	190,972	110,527	109,532	131,227	138,897	106,931	67,856

## BUSINESS

## GENERAL

We are a biopharmaceutical company that discovers, develops and intends to commercialize therapeutic drugs for the treatment of serious medical conditions. Our product pipeline includes drug candidates for the treatment of obesity, rheumatoid arthritis and other inflammatory conditions, cancer and related disorders, allergies, asthma, and other diseases and disorders.

Our core business strategy is to combine our strong foundation in science and technology with state-of-the-art manufacturing and clinical development capabilities to build a successful integrated biopharmaceutical company. Our efforts have yielded a diverse and growing pipeline of product candidates that have the potential to address a variety of unmet medical needs. A key aspect of our strategy is to retain significant ownership and commercialization rights to our pipeline. The ability to participate in the commercialization of our products will enable us to retain the majority of the potential economic rewards from discovering and developing our pipeline. Longer-term, we will continue to invest in the development of additional enabling technologies to assist in our efforts to identify, develop, and commercialize new product candidates.

## OUR INDEPENDENT PROGRAMS

The following table lists the product candidates and programs for which we retain sole ownership and marketing rights.

PROGRAM AND PRODUCT CANDIDATE -----	TARGETED INDICATION -----	STAGE -----
AXOKINE(R)	Obesity	Clinical
PEGYLATED AXOKINE	Obesity	Preclinical
IL-1 TRAP	Rheumatoid arthritis	Clinical
IL-4/13 TRAP	Asthma and allergic disorders	Preclinical
TRAPS FOR IL-2, IL-3, IL-4, IL-5, IL-6, IL-15, GAMMA-INTERFERON, TGF-BETA AND OTHERS	Multiple disease states	Research
VEGF TRAP	Cancer	Preclinical
ANGIOPOIETIN-1	Vascular leak and edema	Preclinical
EPHRINS, ANGIOPOIETIN-2	Cancer and ischemia	Research
REGENERON ORPHAN RECEPTORS (RORS)	Osteoarthritis and other cartilage diseases	Research

AXOKINE. AXOKINE is our patented second generation ciliary neurotrophic factor, called CNTF. We are developing AXOKINE for the treatment of obesity.

Obesity is a major health problem in all developed countries. The prevalence of obesity in the United States has increased substantially during the past decade. A 1999 Congressional Report funded by the National Institutes of Health confirmed that obesity significantly increases a number of health risks, including Type II diabetes. Obesity-related conditions, such as stroke and myocardial infarct are estimated to contribute to about 300,000 deaths yearly, ranking second only to smoking as a cause of preventable death. Health care expenditures for obesity-related conditions now total over \$200 billion a year in the United States. Current treatment of obesity consists of diet, exercise and other lifestyle changes, and a limited number of drugs. There are two approved drugs currently indicated for the treatment of obesity -- sibutramine (Meridia(R)) and orlistat (Xenical(R)). According to their approved product labels, over a twelve-month treatment period, these drugs, at their approved starting doses, have produced weight loss of between approximately five and nine pounds as compared to patients taking placebo.

In November 2000, we announced the preliminary results of a Phase II clinical trial, which tested the safety and efficacy of AXOKINE in severely obese patients. This Phase II trial was a randomized, double-blind, placebo-controlled, out-patient study conducted at seven sites in the United States. Following an initial two-week "run-in period," all subjects received 12 weeks of daily treatment, administered under the skin by patient self-injection. A total of 170 patients were divided into five patient groups. The first four patient groups comprised the pre-specified population for the primary analyses and received placebo, a daily dose of 0.3 micrograms (mcg) per kilogram (kg) of AXOKINE, a daily dose of 1.0 mcg/kg, and a daily dose of 2.0 mcg/kg, respectively, in each case, over the twelve-week treatment period. A fifth group received a daily dose of 1.0 mcg/kg for eight weeks, followed by a blinded withdrawal period in which they received placebo for four weeks. The pre-specified end points of the study were change in weight for the patients who completed the full twelve weeks of treatment ("Completer Analysis"), as well as change in weight for all patients, whether or not they completed the full twelve weeks of treatment ("Last Observed Value Analysis"). All AXOKINE-treated groups showed medically meaningful and statistically significant weight loss compared to placebo. Summarized below are the results of the four groups comprising the primary analyses.

## COMPLETER ANALYSIS

	MEAN WEIGHT CHANGE FROM BASELINE (POUNDS)	p VALUE (RELATIVE TO PLACEBO)
	-----	-----
Placebo (n=19)	+1.3	--
0.3 mcg/kg (n=23)	-3.4	p = 0.01
1.0 mcg/kg (n=26)	-8.9	p < 0.0001
2.0 mcg/kg (n=19)	-7.5	p < 0.0001

## LAST OBSERVED VALUE ANALYSIS

	MEAN WEIGHT CHANGE FROM BASELINE (POUNDS)	p VALUE (RELATIVE TO PLACEBO)
	-----	-----
Placebo (n=31)	+0.6	--
0.3 mcg/kg (n=31)	-2.4	p = 0.04
1.0 mcg/kg (n=37)	-7.5	p < 0.0001
2.0 mcg/kg (n=33)	-5.8	p < 0.0001

As used in the table above, the term "n" refers to the number of patients in each patient group. The reference to "p" value (relative to placebo) means the probability of being wrong when asserting that a true difference exists between the results for the patient group in question and the placebo group. For example, a p-value of less than 0.0001 is a less than one in ten thousand chance of the values observed in the group treated with drug and the group treated with placebo being the same.

The trial established the optimal dose of AXOKINE to be 1.0 mcg/kg daily. Patients who received the optimal dose of AXOKINE over the 12 week treatment period averaged 10 pounds more weight loss than patients on placebo. Moreover, 46% of these patients in the optimal dose group lost at least 10 pounds, compared to just 5% of the patients who received placebo. Nausea was shown not to be a factor that determined average weight loss in this Phase II Study.

The 38 patients in the fifth group who received 1 mcg/kg of daily AXOKINE for eight weeks followed by the four week blinded withdrawal period lost weight during the treatment period and did not regain weight while taking placebo.

No serious adverse events associated with the drug were reported during the trial and the drug was generally well tolerated, as reflected by the following ratio of patients in each treatment group completing the full twelve weeks of treatment according to the protocol: placebo, 61%; 0.3 mcg/kg, 74%; 1.0 mcg/kg, 70%, and 2.0 mcg/kg, 58%. The most common side effect was dose-dependent injection site reactions (skin redness), which occurred in all patient groups, including placebo, and were generally mild. Other side effects associated with the drug included cough and vomiting, which were notable only in the 2.0 mcg/kg dose group, and nausea, which occurred most frequently in the 2.0 mcg/kg dose group. There was no increase compared to placebo in the incidence of herpes simplex infections in patients taking

AXOKINE. Neutralizing antibodies, based on a laboratory test, were not dose-related and occurred in less than 10% of all patients receiving AXOKINE.

Subject to discussions with the FDA, we intend to initiate Phase III testing of AXOKINE in severely obese patients in mid-2001. This Phase III study likely will involve the enrollment of several thousand severely obese patients with a treatment period of at least two years.

In March 2000, we established a research and development collaboration with Emisphere Technologies, Inc. to utilize Emisphere's oral drug delivery technology for AXOKINE. In preliminary preclinical pharmacokinetic studies, the Emisphere technology was able to achieve measurable blood levels of AXOKINE.

PEGYLATED AXOKINE. We are developing a pegylated version of AXOKINE (pegAXOKINE) as a more potent, long-acting form of the protein. PegAXOKINE may allow for less frequent and/or lower dosing in patients. PegAXOKINE currently is in late-stage preclinical development and we anticipate initiating a Phase I clinical trial in mid-2001. Shearwater Corporation has contracted with us to develop and supply the pegylated reagent for this product candidate.

CYTOKINE TRAPS. Our research on the CNTF class of neurotrophic factors led to the discovery that CNTF, although it is a neurotrophic factor, belongs to the "superfamily" of factors referred to as cytokines. Cytokines are soluble proteins secreted by the cells of the body. In many cases, cytokines act as messengers to help regulate immune and inflammatory responses. In excess, cytokines can be harmful and have been linked to a variety of diseases. Blocking cytokines and growth factors is a proven therapeutic approach with a number of drugs already approved or in clinical development. The cytokine superfamily includes factors such as erythropoietin, thrombopoietin, granulocyte-colony stimulating factor and the interleukins (or ILs).

In 1994, our scientists made a breakthrough in understanding how receptors work for an entire class of interleukins in the human body. Based on this finding, we developed a family of antagonists, which are compounds that block a receptor, referred to as "Cytokine Traps." This includes Cytokine Traps for IL-1, IL-4, and IL-6, and a single Trap that blocks both IL-4 and IL-13. Because these Traps mimic the body's natural receptors, they are effective at catching and holding the cytokines. With cytokines trapped, the immune system responds as if the perceived threat is under control.

In preclinical studies, these Cytokine Traps are more potent than other antagonists, potentially allowing lower levels of the drug to be used. Moreover, because these Cytokine Traps are comprised entirely of natural human-derived sequences they may be less likely to induce an immune reaction in humans. Because pathological levels of IL-1, IL-4, IL-6 and IL-13 seem to contribute to a variety of disease states, these Cytokine Traps have the potential to be important therapeutic agents.

IL-1 TRAP. In December 2000, we initiated a Phase I study of the IL-1 Trap to assess its safety and tolerability in patients with rheumatoid arthritis. The placebo-controlled, double-blind, dose-escalation study is being conducted at several centers in the United States and includes a single dose phase and a multiple dose phase. We expect the study to be completed in the second half of 2001. The IL-1 Trap is being evaluated for potential uses to treat other inflammatory diseases as well.

Rheumatoid arthritis is a chronic disease in which the immune system attacks the tissue that lines and cushions joints. Over time, the cartilage, bone, and ligaments of the joint erode, leading to progressive joint deformity and joint destruction, generally in the hand, wrist, knee, and foot. Joints become painful and swollen and motion is limited. Over time, the cartilage erodes, resulting in structural damage to the joint. Over two million people, 1% of the U.S. population, are estimated to have rheumatoid arthritis, and 10% of those eventually become disabled. Women account for two-thirds of these patients.

Rheumatoid arthritis involves an excess of certain cytokines, including IL-1 and tumor necrosis factor (TNF). Drugs that block TNF have already been approved for the treatment of rheumatoid arthritis, while animal studies indicate that IL-1 is also an attractive target for drug development in this disease. In

animal models, our IL-1 Trap is a potent blocker of IL-1 activity, has a long half-life in the blood, penetrates into the inflamed joint, and blocks cartilage erosion in animal models.

While both TNF and IL-1 can induce arthritis, IL-1 more potently induces cartilage destruction in animal models. In addition, the arthritis caused by TNF in some animals can be prevented by blocking the action of IL-1, indicating that the arthritogenic action of TNF may be mediated in part through IL-1. Even stronger evidence for the role of IL-1 in rheumatoid arthritis is that mice that are deficient in the interleukin-1 receptor antagonist (IL-1-ra), a naturally occurring blocker of IL-1 action, develop spontaneously occurring arthritis. The validation of IL-1 blockade as a target for drugs to treat rheumatoid arthritis also appears to have been demonstrated by the positive results reported by another company with administration of IL-1-ra in clinical trials to patients with rheumatoid arthritis.

**IL-4/IL-13 TRAP.** Antagonists for IL-4 and IL-13 may be therapeutically useful in a number of allergy and asthma-related conditions, including vaccination settings in which blocking IL-4 and IL-13 may help elicit more of the desired type of immune response to the vaccine. We have developed both an IL-4 Trap and an IL-4/IL-13 Trap which is a single molecule that can block both interleukin-4 and interleukin-13. We expect to initiate a clinical trial of a dual IL-4/IL-13 Trap to assess its safety and tolerability for the treatment of asthma/allergy related conditions late in 2001.

One in 13 Americans suffers from allergies and one in 18 suffers from asthma. The number of people afflicted with these diseases has been growing at an alarming rate. It is believed that IL-4 and IL-13 play a role in these diseases. These two cytokines are essential to the normal functioning of the immune system, creating a vital communication link between white blood cells. In the case of asthma and allergies, however, there are too many interleukins present, causing the immune system to overact. Therefore, our IL-4/IL-13 Trap may offer unique advantages over other products and product candidates for asthma and allergy related conditions because of its ability to block both of the cytokines thought to be at the root of these disorders.

**OTHER CYTOKINE TRAPS.** Another Cytokine Trap in preclinical development is for IL-6. IL-6 has been implicated in the pathology and progression of multiple myeloma, certain solid tumors, AIDS, lymphomas (both AIDS-related and non-AIDS-related), osteoporosis, and other conditions. We also have patents covering additional Cytokine Traps for IL-2, IL-3, IL-5, IL-15, gamma-interferon, transforming growth factor beta, and others, which are being pursued at the research level. Our research regarding protein-based cytokine antagonists currently includes molecular and cellular research to improve or modify Cytokine Trap technology, process development efforts to produce experimental and clinical research supplies, and in vivo and in vitro studies to further understand and demonstrate the efficacy of the Cytokine Traps.

**VEGF TRAP AND ANGIOPOIETINS.** A plentiful blood supply is required to nourish every tissue and organ of the body. Diseases such as diabetes and atherosclerosis wreak their havoc, in part, by destroying blood vessels (arteries, veins and capillaries) and compromising blood flow. Decreases in blood flow (known as ischemia) can result in non-healing skin ulcers and gangrene, painful limbs that cannot tolerate exercise, loss of vision and heart attacks. In other cases, disease processes can damage blood vessels by breaking down vessel walls, resulting in defective and leaky vessels. Leaking vessels can lead to swelling and edema, as occurs in brain tumors following ischemic stroke, in diabetic retinopathy, and in arthritis and other inflammatory diseases. Finally, some disease processes such as tumor growth depend on the induction of new blood vessels.

Depending on the clinical situation, positively or negatively regulating blood vessel growth could have important therapeutic benefits, as could the repair of damaged and leaky vessels. Thus, building new vessels, by a process known as angiogenesis, can improve circulation to ischemic limbs and heart, aid in healing of skin ulcers or other chronic wounds and in establishing tissue grafts. Reciprocally, blocking tumor-induced angiogenesis can blunt tumor growth. In addition, repairing leaky vessels can reverse swelling and edema.

Vascular endothelial growth factor (VEGF) was the first growth factor shown to be specific for blood vessels, by virtue of having its receptor specifically expressed on blood vessel cells. Our scientists discovered a second family of angiogenic growth factors, termed the Angiopoietins, and we have received patents for the members of this family. The Angiopoietins include naturally occurring positive and negative regulators of angiogenesis, as described in numerous scientific manuscripts published by our scientists and their collaborators.

Our studies have revealed that VEGF and the Angiopoietins normally function in a coordinated and collaborative manner during blood vessel growth. Thus, the growth of new blood vessels to nourish ischemic tissue appears to require use of both these agents. In addition, Angiopoietin-1 seems to play a critical role in stabilizing the vessel wall, and the use of this growth factor can prevent or repair leaky vessels in animal models. In terms of blocking vessel growth, both VEGF and Angiopoietin manipulation seem to be of value.

Currently, we have a highly potent VEGF antagonist, termed the VEGF Trap, in preclinical development as an anti-angiogenic agent for cancer. We expect to begin a clinical trial of the VEGF Trap as a potential treatment for harmful angiogenesis or vascular leak in settings of cancer and/or other conditions in mid-2001. In addition, we are evaluating Angiopoietin-1 and engineered designer versions in preclinical studies to determine its utility for blocking blood vessel leak and for growing blood vessels in ischemia.

We and others have identified a family of growth factors termed the Ephrins and their receptors termed the Ephs. Members of this family have specific roles in angiogenesis and hemopoiesis, which are being pursued in preclinical studies.

**CARTILAGE GROWTH FACTOR SYSTEM AND OSTEOARTHRITIS.** Osteoarthritis results from the wearing down of the articular cartilage surfaces that cover joints. Thus, growth factors that specifically act on cartilage cells could have utility in osteoarthritis. Our scientists have discovered a growth factor receptor system selectively expressed by cartilage cells, termed Regeneron Orphan Receptor 2 (ROR2). Furthermore, our scientists have demonstrated that this growth factor receptor system is required for normal cartilage development in mice. In addition, together with collaborators, our scientists have proven that mutations in this growth factor receptor system cause inherited defects in cartilage development in humans. Thus, this growth factor receptor system is a promising new target for cartilage diseases such as osteoarthritis.

#### OUR COLLABORATIVE PROGRAMS

**MUSCLE ATROPHY AND RELATED DISORDERS.** Muscle atrophy occurs in many neuromuscular diseases and also when muscle is unused, as often occurs during prolonged hospital stays and during convalescence. Currently, physicians have few options to prescribe for patients with muscle atrophy or other muscle conditions which afflict millions of patients globally. Thus, a factor that might have beneficial effects on skeletal muscle could have significant clinical benefit. Our muscle program is currently focused on conducting in vivo and in vitro experiments with the objective of demonstrating and further understanding the molecular mechanisms involved in muscle atrophy and hypertrophy. This work is being conducted in collaboration with scientists at Procter & Gamble as part of our collaboration.

**NT-3.** Amgen-Regeneron Partners' clinical development of NT-3 is currently focused on the treatment of constipating conditions. In 1998, we, on behalf of Amgen-Regeneron Partners, completed a small clinical study that included healthy volunteers and patients suffering from severe idiopathic constipation. We also conducted additional small studies in patients who suffer from constipation associated with conditions such as spinal cord injury and the use of narcotic analgesics. In 2000, we initiated double-blind, placebo-controlled Phase II studies of NT-3 in patients with functional constipation and spinal cord injury patients with bowel dysfunction. These studies currently are underway and we expect them to be completed in mid-2001. Amgen-Regeneron Partners is developing NT-3 in the United States under a license from Takeda Chemical Industries, Ltd.

**OTHER EARLY STAGE PROGRAMS: FIBROSIS AND G-PROTEIN COUPLED RECEPTORS.** Fibrotic diseases, such as cirrhosis, result from the excess production of fibrous extracellular matrix by certain cell types that are inappropriately activated in these diseases. We and our collaborators identified orphan receptors, termed Discoidin Domain Receptors 1 and 2 (DDR1 and DDR2), that are expressed by the activated cell types in fibrotic disease. We have further shown that these receptors bind and are activated by the fibrous matrix they produce. Thus, these receptors are important new targets in fibrotic disease.

We also have an intensive program to discover and characterize G-Protein Coupled Receptors, which have historically been among the most useful targets for pharmaceuticals.

The work in fibrotic diseases and certain G-Protein Coupled Receptors is being conducted in collaboration with scientists at Procter & Gamble as part of our collaboration.

#### OUR TECHNOLOGY PLATFORMS

Our ability to discover and develop product candidates for a wide variety of serious medical conditions results from the leveraging of our powerful technology platforms, many of which were developed or enhanced by us. Although the primary use of these technology platforms is for our own research and development programs, we are also exploring the possibilities of exploiting these technologies commercially through, for example, the direct licensing or sale of technology, or the establishment of research collaborations to discover and develop drug targets.

**TARGETED GENOMICS(TM).** In contrast to basic genomics approaches, which attempt to identify every gene in a cell or genome, we use Targeted Genomics approaches to identify specific genes likely to be of therapeutic interest. These approaches do not depend on random gene sequencing, but rather on function-based approaches, to specifically target the discovery of genes for growth factors, peptides, and their receptors that are most likely to have use for developing drug candidates. This technology has already led to our discovery of Angiotensin and Ephrin growth factor families for angiogenesis and vascular disorders, the MuSK growth factor receptor system for muscle disorders, and the Regeneron Orphan Receptor (ROR) growth factor receptor system that regulates cartilage formation.

**HIGH THROUGHPUT FUNCTIONOMICS(TM):** A major challenge facing the biopharmaceutical industry in the post-genomic era involves the efficient assignment of function to random gene sequences to enable the identification of validated drug targets. One way to help determine the function of a gene is to generate mice in which the gene is removed (referred to as "knockout mice"), or is over-produced (referred to as "transgenic mice"), or in which a color-producing gene is substituted for the gene of interest (referred to as "reporter knockin mice") to identify which cells in the body are expressing the gene. Until recently, technical hurdles involved in the generation of mouse models restricted the ability to produce multiple models quickly and efficiently. We have developed proprietary technology, which we believe will allow for the rapid and efficient production of genetically modified mice in a high throughput scale enabling rapid assignment of function to gene sequences.

**DESIGNER PROTEIN THERAPEUTICS(TM):** In cases in which the natural gene product is itself not a product candidate, we utilize our Designer Protein Therapeutics platform to genetically engineer product candidates with the desired properties. We use these technologies to develop derivatives of growth factors and their receptors, which can allow for modified agonistic or antagonistic properties that may prove to be therapeutically useful. Examples include the generation of AXOKINE, and the development of Cytokine Traps and the VEGF Trap. This technology platform has already produced more than 10 patented proteins, including the IL-1 Trap currently in Phase I clinical testing, and several others in preclinical development.

#### COLLABORATIVE RELATIONSHIPS

We currently conduct programs in collaboration with academic and corporate partners and independently. We have entered into research collaboration and licensing agreements with various corporate partners, including Procter & Gamble, Amgen and Sumitomo Pharmaceuticals.

PROCTER & GAMBLE. In May 1997, we entered into a long-term collaboration agreement with Procter & Gamble to discover, develop, and commercialize pharmaceutical products. Procter & Gamble agreed over the first five years of the 1997 collaboration to purchase up to \$60.0 million of our equity, of which \$42.9 million was purchased in June 1997 and \$17.1 million was purchased in August 2000. These equity purchases were in addition to a purchase by Procter & Gamble of \$10.0 million of our common stock that was completed in March 1997. Procter & Gamble also agreed over the first five years of the 1997 collaboration to provide funding in support of our research efforts related to the collaboration, of which we had received \$38.0 million through September 30, 2000. In August 2000, Procter & Gamble made two non-recurring research progress payments to us totaling \$3.5 million. In addition, in August 2000, we and Procter & Gamble agreed through a binding memorandum of understanding to enter into a new collaboration agreement, replacing the companies' 1997 collaboration agreement. The new agreement extends Procter & Gamble's obligation to fund our research under the new collaboration agreement through December 2005, with no further research obligations by either party thereafter, and focuses the companies' collaborative research on therapeutic areas that are of particular interest to Procter & Gamble, including muscle atrophy and muscle diseases, fibrotic diseases, and certain G-Protein Coupled Receptors.

We and Procter & Gamble have divided rights to the programs from the 1997 collaboration agreement that are no longer part of the companies' collaboration. Procter & Gamble has obtained rights to certain specified programs. We have rights to all other research programs including exclusive rights to the VEGF Trap, the Angiopoietins and Regeneron's Orphan Receptors (RORs). Any drugs that result from the new collaboration will continue to be jointly developed and marketed worldwide, with the companies equally sharing development costs and profits. Under the original 1997 collaboration agreement, research support from Procter & Gamble would have been \$6.8 million per quarter (before adjustments for future inflation) for the period from July 2000 through June 2002. Under the new agreement, beginning in the first quarter of 2001, research support from Procter & Gamble will be \$2.5 million per quarter (before adjustments for future inflation) through December 2005, and total funding from July 2000 through December 2005 will be approximately \$64 million.

In addition to certain termination rights, our new collaboration agreement with Procter & Gamble has an "opt-out" provision, whereby a party may decline to participate further in a research or product development program. In such cases, the opting-out party will generally not have any further funding obligation and will not have any rights to the product or program in question (but may be entitled to a royalty on any product sales). If Procter & Gamble opts out of a product development program, and we do not find a new partner, we would bear the full cost of the program.

After examining the interim data from the Phase I study of AXOKINE completed in 1999, Procter & Gamble decided to return to us the product rights to AXOKINE. However, under certain circumstances, Procter & Gamble will be entitled to receive a small royalty on any sales of AXOKINE.

MEDAREX. In March 2000, we entered into a collaboration under a binding memorandum of understanding with Medarex, Inc. to discover, develop and commercialize human antibodies as therapeutics. We will contribute our expertise in discovering and characterizing proteins as drug targets, and Medarex will contribute its HuMab-Mouse(TM) technology to create fully human antibody products for those targets. Together we have selected more than twenty initial targets, including growth factors, cytokines, and receptors, and plan to add additional targets in the future. We and Medarex intend to prioritize targets based upon a variety of criteria, including target validation, reagent availability, market opportunity, competitive factors, intellectual property position, and the expected feasibility of obtaining antibodies that have the desired properties. The HuMab-Mouse is a transgenic mouse whose genes for creating mouse antibodies have been inactivated and replaced by human antibody genes. This makes it possible to rapidly create and develop fully human antibodies as drug candidates. We and Medarex agreed to share preclinical and clinical responsibilities and intend to jointly market any drugs that result from this collaboration.

EMISPHERE. In March 2000, we signed an agreement with Emisphere Technologies, Inc. to establish a research and development collaboration to utilize Emisphere's oral drug delivery technology for AXOKINE. In preliminary preclinical pharmacokinetic studies, the Emisphere technology was able to achieve measurable blood levels of AXOKINE. Under the terms of the agreement, we will support research at Emisphere and under certain conditions will make additional payments, including license and milestone payments. We will receive exclusive worldwide commercialization rights to oral products that result from the collaboration and pay Emisphere a royalty on sales of any such products.

SHEARWATER. In December 2000, we entered into a license and supply agreement with Shearwater Corporation under which Shearwater will develop and supply a pegylated reagent that could be used to formulate a modified form of AXOKINE. In preclinical studies, a pegylated AXOKINE was substantially longer lasting than unmodified AXOKINE. This may allow less frequent and lower dosing in patients. Under the terms of the agreement, Shearwater will develop and supply the reagent and we will manufacture and have exclusive rights to pegylated AXOKINE. Shearwater is entitled to receive milestone payments based on the development of the modified AXOKINE and will be the exclusive supplier of the reagent. We will pay Shearwater a royalty not to exceed 2.5% on sales of any pegylated AXOKINE.

AMGEN. We are conducting clinical trials of NT-3 on behalf of Amgen-Regeneron Partners, a general partnership owned equally by us and Amgen. We are required to fund 50% of the development costs of Amgen-Regeneron Partners to maintain 50% of the commercialization rights. Assuming equal capital contributions to Amgen-Regeneron Partners, we and Amgen share any profits or losses of Amgen-Regeneron Partners equally. Under our agreement with Amgen we are attempting to develop with Amgen and, if such effort is successful, commercialize, market and distribute NT-3 in the United States through Amgen-Regeneron Partners.

The development and commercialization of NT-3 outside of the United States, Japan, China, and certain other Pacific Rim countries, if any, will be conducted solely by Amgen through a license from us and from Takeda Chemical Industries, Ltd. In return, we will receive royalty payments based on Amgen's net sales of any products in the licensed territory. In the licensed territory, Amgen is solely responsible for funding clinical development and related costs of the licensed products, as well as costs of their commercial exploitation, and has sole discretion with respect to all such development, manufacturing and marketing of the products and sole responsibility for filing applications for regulatory approvals.

Following a review of available clinical trial data, we and Amgen recently discontinued the development of BDNF for the treatment of amyotrophic lateral sclerosis (or ALS).

SUMITOMO. In connection with a \$4.4 million equity investment made by Sumitomo Chemical Company, Ltd. in March 1989, we granted Sumitomo Chemical a limited right of first negotiation to license up to three of the product candidates we decide to commercialize in Japan (one of which has been exercised to date) on financial and commercial terms as we may offer. We are obligated periodically to inform and, if requested, to meet with Sumitomo Chemical management about our progress in research and development.

OTHER AGREEMENTS. We have agreements with individual researchers and universities to conduct sponsored research and development programs. The goal of these agreements is to extend our capabilities and to acquire proprietary rights to the results of sponsored research. We are party to a number of sponsored research agreements which include grants to us of exclusive licenses to certain discoveries and technologies developed at, among other places, the Max Planck Institute and the University of California at San Francisco. We have also collaborated with Glaxo SmithKline plc to discover and develop small molecule-based treatments for neurodegenerative diseases. In addition to these sponsored research agreements, we (individually or in partnership with our collaborators) provide research material and information that relate to our product candidates and research programs to over 400 investigators at private and public institutions throughout the world. We provide supplies, materials and know-how to these investigators on a confidential basis in exchange for access to additional research and ownership of certain proprietary rights resulting from the work of the investigators.

**MANUFACTURING**

We maintain an 8,000 square foot manufacturing facility in Tarrytown, New York. This facility, which was designed to comply with FDA current good manufacturing practices (called GMP), produces preclinical and clinical supplies of our product candidates.

In 1993, we purchased our 100,000 square foot Rensselaer, New York manufacturing facility, which is being used to manufacture drugs for our own preclinical and clinical studies. We also use the facility to manufacture a product for Merck under a long-term contract.

Currently we dedicate approximately 200 people to our manufacturing operations at these facilities.

**PATENTS, TRADEMARKS AND TRADE SECRETS**

Our success depends, in part, on our ability to obtain patents, maintain trade secret protection and operate without infringing on the proprietary rights of third parties. Our policy is to file patent applications to protect technology, inventions, and improvements that are considered important to the development of our business. We have been granted 45 U.S. patents and we have more than 100 pending applications. We are the exclusive or nonexclusive licensee of a number of additional U.S. patents and patent applications. We also rely upon trade secrets, know-how, and continuing technological innovation to develop and maintain our competitive position. We or our licensors or collaborators have filed patent applications on products and processes relating to neurotrophic factors and other technologies and inventions in the United States and in certain foreign countries. We intend to file additional patent applications, when appropriate, relating to improvements in these technologies and other specific products and processes. We plan to aggressively prosecute, enforce, and defend our patents and other proprietary technology.

In September 2000, Immunex Corporation filed a request with the European Patent Office seeking the declaration of an Opposition regarding our European patent relating to Cytokine Traps. This is a legal challenge to the validity and scope of our patent. Although we plan to defend the patent diligently, we cannot predict whether the scope of the patent will be affected in the future should an Opposition be declared.

**EMPLOYEES**

As of December 31, 2000, we had 491 full-time employees, 85 of whom hold a Ph.D. or M.D. degree or both. We believe that we have been successful in attracting skilled and experienced personnel in a highly competitive environment.

## MANAGEMENT

## DIRECTORS AND EXECUTIVE OFFICERS

The following table provides information with respect to our directors and executive officers as of December 31, 2000:

NAME - - - - -	AGE ---	POSITION -----
P. Roy Vagelos, M.D.....	71	Chairman of the Board of Directors (Class II)
Leonard S. Schleifer, M.D., Ph.D. ....	48	Director (Class I), President, Chief Executive Officer and Founder
George D. Yancopoulos, M.D., Ph.D. ....	41	Executive Vice President and Chief Scientific Officer and President, Regeneron Research Laboratories
Murray A. Goldberg.....	55	Senior Vice President, Finance & Administration, Chief Financial Officer, Treasurer, and Assistant Secretary
Randall G. Rupp, Ph.D. ....	53	Senior Vice President, Manufacturing and Process Sciences
Neil Stahl, Ph.D. ....	44	Senior Vice President, Preclinical Development and Biomolecular Science
Charles A. Baker.....	68	Director (Class III)
Michael S. Brown, M.D. ....	59	Director (Class III) and Member of Scientific Advisory Board
Alfred G. Gilman, M.D., Ph.D. ....	59	Director (Class II), Member of Scientific Advisory Board and Co-Founder
Joseph L. Goldstein, M.D. ....	60	Director (Class II) and Member of Scientific Advisory Board
Fred A. Middleton.....	51	Director (Class I)
Eric M. Shooter, Ph.D. ....	76	Director (Class I), Member of Scientific Advisory Board and Co-Founder
George L. Sing.....	51	Director (Class III)

The Board of Directors is divided into three classes, denominated Class I, Class II and Class III, with members of each class holding office for staggered three-year terms. Our Class I Directors will stand for election in 2001. Our Scientific Advisory Board consists of individuals with recognized expertise in neurobiology, clinical neurology, molecular biology and related fields who advise us about present and long-term scientific planning, research and development.

P. ROY VAGELOS, M.D., 71, has been chairman of the board of our company and a member of the Scientific Advisory Board since January 1995. He became a part-time employee of Regeneron in January 1999. Prior to joining Regeneron, Dr. Vagelos was Chairman of the Board and Chief Executive Officer of Merck & Co., Inc. He joined Merck in 1975, became a director in 1984, President and Chief Executive Officer in 1985 and Chairman in 1986. Dr. Vagelos retired from all positions with Merck in 1994. Dr. Vagelos is the President and Chief Executive Officer and a Trustee of the American School of Classical Studies at Athens. He is also currently a member of the Board of Directors of The Prudential Insurance Company.

LEONARD S. SCHLEIFER, M.D., Ph.D., 48, founded our company in 1988 and has been its President and Chief Executive Officer since its inception and served as Chairman of the Board from 1990 through 1994. In 1992, Dr. Schleifer was appointed Clinical Professor of Neurology at the Cornell University Medical School and from 1984 to 1988 he was Assistant Professor at the Cornell University Medical School in the Departments of Neurology and Neurobiology. Dr. Schleifer received his M.D. and Ph.D. in Pharmacology from the University of Virginia. Dr. Schleifer is a licensed physician and is certified in Neurology by the American Board of Psychiatry and Neurology.

GEORGE D. YANCOPOULOS, M.D., PH.D., 41, Executive Vice President and Chief Scientific Officer and President, Regeneron Research Laboratories, was until December 2000 our Senior Vice President, Research, a position he held since June 1997 and Chief Scientific Officer, a position he held since January 1998. Dr. Yancopoulos was Vice President, Discovery from January 1992 until June 1997, Head of Discovery from January 1991 to January 1992 and Senior Staff Scientist from March 1989 to January 1991. He received his Ph.D. in Biochemistry and Molecular Biophysics and his M.D. from Columbia University. In a 1997 survey by the Institute for Scientific Information, he was listed among the 11 most highly cited scientists and was the only non-academic scientist in that group.

MURRAY A. GOLDBERG, 55, Senior Vice President, Finance and Administration, Chief Financial Officer, Treasurer, and Assistant Secretary, was until December 2000 our Vice President, Finance and Administration, Chief Financial Officer and Treasurer, a position he held since March 1995, and Assistant Secretary, a position he held since January 2000. Prior to joining us, Mr. Goldberg was Vice President, Finance, Treasurer and Chief Financial Officer of PharmaGenics, Inc. from February 1991 and a Director of that company from May 1991. From 1987 to 1990, Mr. Goldberg was Managing Director, Structured Finance Group at the Chase Manhattan Bank, N.A. and from 1973 to 1987 he served in various managerial positions in finance and corporate development at American Cyanamid Company.

RANDALL G. RUPP, PH.D., 53, Senior Vice President, Manufacturing and Process Sciences, was until December 2000 our Vice President, Manufacturing and Process Science, a position he held since January 1992. Dr. Rupp was our director of manufacturing from July 1991 until December 1992. He received his Ph.D. in Biomedical Sciences from the University of Texas, M.D. Anderson Hospital and Tumor Institution, Houston.

NEIL STAHL, PH.D., 44, Senior Vice President, Preclinical Development and Biomolecular Science, was until December 2000 our Vice President, Preclinical Development and Biomolecular Sciences, a position he held since January 2000. He joined us in 1991. Before becoming Vice President, Biomolecular Sciences in July 1997, Dr. Stahl was Director, Cytokines and Signal Transduction. Dr. Stahl received his Ph.D. in Biochemistry from Brandeis University.

CHARLES A. BAKER, 68, has been a director of our company since February of 1989. In September of 2000, Mr. Baker retired as Chairman, President, and Chief Executive Officer of The Liposome Company, Inc., a position he had held since December of 1989. During his career, Mr. Baker served in a senior management capacity in various pharmaceutical companies, including his tenures as Group Vice President, Squibb Corporation (now Bristol-Myers Squibb) and President, Squibb International. He also held various senior executive positions at Abbott Laboratories and Pfizer, Inc. Mr. Baker currently is a member of the Board of Directors of Progenics Pharmaceuticals, Inc. and a member of the Council of Visitors of the Marine Biological Laboratories at Woods Hole, Massachusetts (a not-for-profit organization). He is also a special limited partner in Sanderling Ventures, which is a shareholder of Regeneron.

MICHAEL S. BROWN, M.D., 59, has been a director of our company since June 1991 and a member of our Scientific Advisory Board since January 1988. Dr. Brown is Professor of Medicine and Genetics and the Director of the Center for Genetic Diseases at The University of Texas Southwestern Medical Center at Dallas. He is a member of the National Academy of Sciences. He is a Director of Pfizer, Inc. His scientific contributions in cholesterol and lipid metabolism were made in collaboration with Dr. Joseph L. Goldstein. Dr. Brown and Dr. Goldstein jointly received the Nobel Prize for Physiology or Medicine in 1985.

ALFRED G. GILMAN, M.D., PH.D., 59, a co-founder of our company, has been a director of our company since July 1990 and a member of our Scientific Advisory Board since 1988. Dr. Gilman has been the Raymond and Ellen Willie Professor of Molecular Neuropharmacology and Chairman of the Department of Pharmacology at The University of Texas Southwestern Medical Center at Dallas since 1981 and was named a Regental Professor in 1995. Dr. Gilman is a member of the National Academy of Sciences. He is the Consulting Editor of "Goodman and Gilman's The Pharmacological Basis of Therapeutics," the leading medical pharmacology textbook. Dr. Gilman received the Nobel Prize for

Physiology or Medicine in 1994. Dr. Gilman is a member of the Board of Directors of Eli Lilly & Company.

JOSEPH L. GOLDSTEIN, M.D., 60, has been a director of our company since June 1991 and a member of our Scientific Advisory Board since January 1988. Dr. Goldstein has been the Professor of Medicine and Genetics and Chairman of the Department of Molecular Genetics at The University of Texas Southwestern Medical Center at Dallas for more than five years. Dr. Goldstein is a member of the National Academy of Sciences. Dr. Goldstein and Dr. Brown jointly received the Nobel Prize for Physiology or Medicine in 1985.

FRED A. MIDDLETON, 51, has been a director of our company since July 1990. Mr. Middleton is a General Partner of Sanderling Ventures, a venture capital firm he co-founded with Dr. Robert McNeil in December 1987 specializing in early stage biomedical companies. Sanderling Ventures is a shareholder of the Company. Between 1984 and 1987, he was Managing General Partner of Morgan Stanley Ventures and, from 1978 through 1984, was Vice President and Chief Financial Officer of Genentech, Inc. and President, Genentech Development Corporation.

ERIC M. SHOOTER, PH.D., 76, a co-founder of our company, has been a director of our company and member of the Scientific Advisory Board since 1988. Dr. Shooter has been a professor at Stanford University School of Medicine since 1968. He was the founding Chairman of the Department of Neurobiology at Stanford University School of Medicine in 1975 and served as its Chairman until 1987. He is a Fellow of the Royal Society of England and a member of the National Academy of Sciences.

GEORGE L. SING, 51, has been a director of our company since January 1988. Since 1998, he has been a Managing Director of Caduceus Capital Partners, a venture capital investment firm in the health care field. From 1993 to 1998 Mr. Sing was a general partner of Zitan Capital Partners, an investment and advisory firm. From February 1990 until February 14, 1991, Mr. Sing served as a consultant to Merrill Lynch Venture Capital Inc. From 1982 to February 1990, Mr. Sing was a Vice President and member of the Board of Directors of Merrill Lynch Venture Capital Inc., a venture capital firm.

#### INVESTMENT COMPANY ACT CONSIDERATIONS

The Investment Company Act of 1940, as amended, requires the registration of, and imposes various substantive restrictions on, certain companies that engage primarily, or propose to engage primarily, in the business of investing, reinvesting or trading in securities, or fail certain statistical tests regarding the composition of assets and sources of income and are not primarily engaged in businesses other than investing, holding, owning, or trading securities. We presently satisfy these statistical tests and intend to remain primarily engaged in businesses other than investing, reinvesting, owning, holding, or trading securities. In addition, we are relying on an SEC position that biotechnology companies such as our company are not investment companies required to register under the 1940 Act. We will seek temporarily to invest the proceeds of this offering, pending their use as described under the caption "Use of Proceeds." We expect to continue to be able to avoid registration requirements of the 1940 Act. If we were required to register as an investment company under the 1940 Act, we would become subject to substantial regulations with respect to our capital structure, management, operations, transactions with affiliates described in the 1940 Act and other matters. Application of the provisions of this Act would have a material adverse effect on our business.

## DESCRIPTION OF CAPITAL STOCK

Our authorized capital stock consists of 60,000,000 shares of common stock, par value \$.001 per share, 40,000,000 shares of Class A stock, par value \$.001 per share, and 30,000,000 shares of preferred stock, par value \$.01 per share. As of January 23, 2001, 34,215,308 shares of our common stock were outstanding and held by 605 shareholders of record and 2,612,845 shares of our Class A stock were outstanding and held by 66 shareholders of record. The following is a summary description of our capital stock. For more information, see our Restated Certificate of Incorporation, a copy of which is incorporated by reference as an exhibit to the registration statement of which this prospectus forms a part.

## COMMON STOCK AND CLASS A STOCK

**General.** The rights of holders of common stock and holders of Class A stock are identical except for voting and conversion rights and restrictions on transferability.

**Voting Rights.** The holders of Class A stock are entitled to ten votes per share and the holders of common stock are entitled to one vote per share. Except as otherwise required by law or as described below, holders of Class A stock will vote together as a single class on all matters presented to the shareholders for their vote or approval, including the election of directors. Shareholders are not entitled to vote cumulatively for the election of directors and no class of outstanding common stock acting alone is entitled to elect any directors.

**Transfer Restrictions.** Class A stock is subject to certain limitations on transfer that do not apply to the common stock.

**Dividends and Liquidation.** Holders of Class A stock and holders of our common stock have an equal right to receive dividends when and if declared by our Board of Directors out of funds legally available therefor. If a dividend or distribution payable in Class A stock is made on the Class A stock, we must also make a pro rata and simultaneous dividend or distribution on the common stock payable in shares of common stock. Conversely, if a dividend or distribution payable in common stock is made on the common stock, we must also make a pro rata and simultaneous dividend or distribution on the Class A stock payable in shares of Class A stock. In the event of our liquidation, dissolution, or winding up, holders of the shares of Class A stock and common stock are entitled to share equally, share-for-share, in the assets available for distribution after payment of all creditors and the liquidation preferences of our preferred stock.

**Optional Conversion Rights.** Each share of Class A stock may, at any time and at the option of the holder, be converted into one fully paid and nonassessable share of common stock. Upon conversion, such shares of common stock would not be subject to restrictions on transfer that applied to the shares of Class A stock prior to conversion except to the extent such restrictions are imposed under applicable securities laws.

The shares of common stock are not convertible into or exchangeable for shares of Class A stock or any other of our shares or securities.

**Other Provisions.** Holders of Class A stock and common stock have no preemptive rights to subscribe to any additional securities of any class which we may issue and there are no redemption provisions or sinking fund provisions applicable to either such class, nor is the Class A stock or the common stock subject to calls or assessments.

**Nasdaq National Market Listing.** Our common stock is quoted on the Nasdaq National Market. The current rules of the National Association of Securities Dealers, Inc. (the "NASD") effectively preclude the trading or quotation through the Nasdaq National Market of any securities of an issuer which has issued securities or taken other corporate action that would have the effect of nullifying, restricting, or disparately reducing the per share voting of an outstanding class or classes of equity securities registered under section 12 of the Exchange Act. Certain national securities exchanges have adopted similar rules or policies. We do not intend to issue any additional shares of any stock that would make it ineligible for

inclusion on the Nasdaq National Market or any national securities exchange. However, if we issue additional stock that causes us to become ineligible for continued inclusion on the Nasdaq National Market, then the ineligibility would be likely to materially reduce the liquidity of an investment in our common stock and would likely depress its market value below that which would otherwise prevail.

Transfer Agent and Registrar. The Transfer Agent and Registrar for the common stock is American Stock Transfer & Trust Company.

#### PREFERRED STOCK

Our Restated Certificate of Incorporation allows us to issue up to 30,000,000 shares of preferred stock in one or more series and as may be determined by our Board of Directors who may establish from time to time the number of shares to be included in each such series, to fix the designation, powers, preference and rights of the shares of each such series and any qualifications, limitations, or restrictions thereof and to increase or decrease the number of shares of any such series without any further vote or action by the shareholders. Our Board of Directors may authorize, without shareholder approval, the issuance of preferred stock with voting and conversion rights that could adversely affect the voting power and other rights of holders of our common stock. Preferred stock could thus be issued quickly with terms designed to delay or prevent a change in control or to make the removal of management more difficult. In certain circumstances, this could have the effect of decreasing the market price of our common stock.

#### REGISTRATION RIGHTS OF CERTAIN HOLDERS

Certain of our shareholders have registration rights. Under the agreements between us and the holders of registration rights, certain holders may under certain circumstances request that we file a registration statement under the Securities Act and, upon such request and subject to certain minimum size conditions, we will generally be required to use our best efforts to effect any such registration. We are not generally required to effect more than two such registrations. However, we are required under certain circumstances to effect an unlimited number of Form S-3 or similar short form registrations for such holders. We are generally obligated to bear the expenses, other than underwriting discounts and sales commissions, of all of these registrations.

In addition, if we propose to register any of our securities, either for our own account or for the account of other shareholders, with certain exceptions, we are required to notify the holders noted above and to include in such registration all of the shares of our common stock requested to be included by such holders.

#### RIGHTS PLAN

In September 1996, we adopted a Shareholder Rights Plan. As with most shareholder rights agreements, the terms of our rights agreement are complex and not easily summarized. This summary may not contain all of the information that is important to you. Accordingly, you should carefully read our rights agreement, which has been filed with the SEC.

Our rights agreement provides that each of our common shares will have one right to purchase a unit consisting of one-thousandth of a preferred share at a purchase price of \$120 per unit.

Initially, the rights under our rights agreement are attached to outstanding certificates representing our common shares and no separate certificates representing the rights will be distributed. The rights will separate from our common shares and be represented by separate certificates approximately 10 days after someone acquires or commences a tender offer for 20% of our outstanding common shares.

After the rights separate from our common shares, certificates representing the rights will be mailed to record holders of our common stock. Once distributed, the rights certificates alone will represent the rights.

All of our common shares issued prior to the date the rights separate from the common shares will be issued with the rights attached. The rights are not exercisable until the date the rights separate from the common shares. The rights will expire on October 18, 2006 unless earlier redeemed or exchanged by us.

If an acquiror obtains or has the right to obtain 20% or more of our common shares, then each right will entitle the holder to purchase a number of our common shares initially equal to two times the purchase price of each right, unless the acquisition is made pursuant to a tender or exchange offer for all of our outstanding shares at a price determined by a majority of our independent directors. In this event, rights held by the acquiring person shall become null and void.

In certain circumstances, a right will entitle the holder to purchase a number of shares of common stock of the acquiror having a then current market value of twice the right's purchase price.

Holders of rights will have no rights as our stockholders including the right to vote or receive dividends, simply by virtue of holding the rights.

Our rights agreement may have anti-takeover effects. The rights may cause substantial dilution to a person or group that attempts to acquire us. Accordingly, the existence of the rights may deter acquirors from making takeover proposals or tender offers. However, the rights are not intended to prevent a takeover, but rather are designed to enhance the ability of our board to negotiate with an acquiror on behalf of all the shareholders. In addition, the rights should not interfere with a proxy contest.

## UNDERWRITING

Merrill Lynch, Pierce, Fenner & Smith Incorporated, J.P. Morgan Securities Inc. and Robertson Stephens, Inc. are acting as representatives of each of the underwriters named below. Subject to the terms and conditions described in a purchase agreement among us and the underwriters, we have agreed to sell to the underwriters and the underwriters severally have agreed to purchase from us the number of shares of common stock listed opposite their names below.

UNDERWRITER -----	NUMBER OF SHARES -----
Merrill Lynch, Pierce, Fenner & Smith Incorporated.....	
J.P. Morgan Securities Inc.....	
Robertson Stephens, Inc.....	
Total.....	4,000,000 =====

The underwriters have agreed to purchase all of the shares sold under the purchase agreement if any of these shares are purchased. If an underwriter defaults, the purchase agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the purchase agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the purchase agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

## COMMISSIONS AND DISCOUNTS

The underwriters have advised us that they propose initially to offer the shares to the public at the public offering price on the cover page of this prospectus and to dealers at that price less a concession not in excess of \$ per share. The underwriters may allow, and the dealers may reallow, a discount not in excess of \$ per share to other dealers. After the public offering, the public offering, price, concession and discount may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their over-allotment options.

	PER SHARE -----	WITHOUT OPTION -----	WITH OPTION -----
Public offering price.....	\$	\$	\$
Underwriting discount.....	\$	\$	\$
Proceeds, before expenses, to Regeneron.....	\$	\$	\$

The expenses of the offering, not including the underwriting discount, are estimated at \$650,000 and are payable by us.

## OVER-ALLOTMENT OPTION

We have granted an option to the underwriters to purchase up to 600,000 additional shares at the public offering price less the underwriting discount. The underwriters may exercise this option for 30 days from the date of this prospectus solely to cover any over-allotments. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the purchase agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

## NO SALES OF SIMILAR SECURITIES

We and our executive officers and directors and certain existing shareholders have agreed, with exceptions, not to sell or transfer any common stock for 90 days after the date of this prospectus without first obtaining the written consent of Merrill Lynch. Specifically, we and these other individuals or entities have agreed not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock;
- sell any option or contract to purchase any common stock;
- purchase any option or contract to sell any common stock;
- grant any option, right or warrant for the sale of any common stock;
- lend or otherwise dispose of or transfer any common stock; and
- enter into any swap or other agreement that transfers, in whole or in part, the economic consequence of ownership of any common stock whether any such swap or transaction is to be settled by delivery of shares or other securities, in cash or otherwise.

This lockup provision applies to common stock and to securities convertible into or exchangeable or exercisable for or repayable with common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

We, however, may issue (1) shares upon the exercise of an option or warrant or the conversion of a security outstanding on the date of this prospectus, (2) shares or options to purchase shares granted pursuant to our existing and future employee benefit plans and (3) shares pursuant to any non-employee director stock plan or dividend reinvestment plan.

The shares are quoted on the Nasdaq National Market under the symbol "REGN."

## UK SELLING RESTRICTIONS

Each underwriter has agreed that

- it has not offered or sold and will not offer or sell any shares of common stock to persons in the United Kingdom, except to persons whose ordinary activities involve them in acquiring, holding, managing or disposing of investments (as principal or agent) for the purposes of their businesses or otherwise in circumstances which do not constitute an offer to the public in the United Kingdom within the meaning of the Public Offers of Securities Regulations 1995;
- it has complied and will comply with all applicable provisions of the Financial Services Act 1986 with respect to anything done by it in relation to the common stock in, from or otherwise involving the United Kingdom; and
- it has only issued or passed on and will only issue or pass on in the United Kingdom any document received by it in connection with the issuance of common stock to a person who is of a kind described in Article 11(3) of the Financial Services Act 1986 (Investment Advertisements) (Exemptions) Order 1996 as amended by the Financial Services Act 1986 (Investment Advertisements) (Exemptions) Order 1997 or is a person to whom such document may otherwise lawfully be issued or passed on.

## NO PUBLIC OFFERING OUTSIDE THE UNITED STATES

No action has been or will be taken in any jurisdiction (except in the United States) that would permit a public offering of the shares of common stock, or the possession, circulation or distribution of this prospectus or any other material relating to us or shares of our common stock in any jurisdiction where action for that purpose is required. Accordingly, the shares of our common stock may not be offered or sold, directly or indirectly, and neither this prospectus nor any other offering material or advertisements in connection with the shares of common stock may be distributed or published, in or from any country or jurisdiction except in compliance with any applicable rules and regulations of any such country or jurisdiction.

Purchasers of the shares offered by this prospectus may be required to pay stamp taxes and other charges in accordance with the laws and practices of the country of purchase in addition to the offering price on the cover page of this prospectus.

## PRICE STABILIZATION, SHORT POSITIONS AND PENALTY BIDS

Until the distribution of the shares of common stock is completed, the SEC rules may limit the underwriters from bidding for or purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases that peg, fix or maintain that price.

The underwriters may purchase and sell the common stock in the open market. These transactions may include short sales, stabilizing transactions, and purchases to cover positions created by short sales. Short sales involve the sale by the underwriters of a greater number of shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares from the issuer in the offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of share to close out the covered 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. "Naked" short sales are any sales in excess of such option. The underwriters must close out any naked short position by purchasing 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 common shares in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the completion of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the underwriters a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales 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 shares of common stock. As a result, the price of the shares of common stock may be higher than the price that might otherwise exist in the open market.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the common stock. In addition, neither we nor any of the representatives make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

## ELECTRONIC PROSPECTUS

Merrill Lynch, Pierce, Fenner & Smith Incorporated will be facilitating Internet distribution for this offering to certain of its Internet subscription customers. Merrill Lynch intends to allocate a limited number of shares for sale to its online brokerage customers. An electronic prospectus is available on the Internet website maintained by Merrill Lynch. Other than the prospectus in electronic format, the information on the Merrill Lynch website is not part of this prospectus.

## PASSIVE MARKET MAKING

In connection with this offering, underwriters and selling group members may engage in passive market making transactions in the common stock on the Nasdaq National Market in accordance with Rule 103 of Regulation M under the Exchange Act during a period before the commencement of offers or sales of common stock and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

## OTHER RELATIONSHIPS

Some of the underwriters and their affiliates have engaged in, and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us. They have received customary fees and commissions for these transactions.

## LEGAL MATTERS

Skadden, Arps, Slate, Meagher & Flom LLP, New York, New York will pass upon the validity of our common stock offered by this prospectus. Shearman & Sterling, New York, New York will pass upon certain legal matters in connection with this offering for the underwriters.

## EXPERTS

The financial statements of Regeneron Pharmaceuticals, Inc. incorporated in this prospectus by reference to the Annual Report on Form 10-K of Regeneron Pharmaceuticals, Inc. for the year ended December 31, 1999, except as they relate to Amgen-Regeneron Partners, have been audited by PricewaterhouseCoopers LLP, independent accountants, and, insofar as they relate to Amgen-Regeneron Partners, by Ernst & Young LLP, independent auditors, whose report thereon is incorporated by reference herein. Such financial statements have been so included in reliance on the report of such independent accountants given on the authority of such firm as experts in auditing and accounting.

Ernst & Young LLP, independent auditors, have audited the financial statements of Amgen-Regeneron Partners included in our Annual Report on Form 10-K for the year ended December 31, 1999, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. The Amgen-Regeneron Partners' financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

## WHERE YOU CAN FIND ADDITIONAL INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any documents we file at the SEC's Public Reference Room at 450 Fifth Street, N.W., Washington, D.C. 20549 and at the Regional Offices of the SEC at 7 World Trade Center, 13th Floor, New York, New York 10048 and Citicorp Center, 500 West Madison Street, Suite 1400, Chicago, Illinois 60601. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. The SEC maintains a site on the World Wide Web at <http://www.sec.gov> that contains our SEC filings and reports, proxy and information statements and other information regarding registrants.

The SEC allows us to "incorporate by reference" the information we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus and information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and all future filings we make with the SEC after the date of the initial registration statement and prior to effectiveness of the registration statement and any filings thereafter and prior to the termination of this offering with the SEC under Section 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934:

- (1) our Annual Report on Form 10-K for the year ended December 31, 1999;
- (2) our Quarterly Reports on Form 10-Q for the quarters ended March 31, 2000, June 30, 2000 and September 30, 2000;
- (3) our Current Reports on Form 8-K filed on March 29, 2000, April 4, 2000, and January 25, 2001; and
- (4) the description of our common stock contained in Item 1 of our Registration Statement on Form 8-A filed on February 20, 1991, as amended by a Form 8 filed on March 27, 1991.

You may request a copy of these filings, at no cost, by writing or telephoning us at the following address:

Regeneron Pharmaceuticals, Inc.  
777 Old Saw Mill River Road  
Tarrytown, New York 10591-6707  
(914) 347-7000  
Attention: Murray A. Goldberg  
Chief Financial Officer

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-----  
4,000,000 SHARES  
REGENERON PHARMACEUTICALS, INC.  
COMMON STOCK

-----  
PROSPECTUS  
-----

MERRILL LYNCH & CO.

JP MORGAN  
ROBERTSON STEPHENS

, 2001  
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## PART II

## INFORMATION NOT REQUIRED IN PROSPECTUS

## ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.

The following table sets forth all fees and expenses in connection with the issuance and distribution of the securities being registered hereby (other than underwriting discounts and commissions). All of such expenses, except the Securities and Exchange Commission registration fee, the National Association of Securities Dealers, Inc. ("NASD") filing fee and the NASDAQ listing fee are estimated.

Securities and Exchange Commission registration fee.....	\$ 39,648.55
NASDAQ listing fee.....	17,500.00
NASD filing fee.....	16,359.42
Legal fees and expenses.....	175,000.00
Transfer Agent and Registrar fees and expenses.....	5,000.00
Accounting fees and expenses.....	165,000.00
Blue sky fees and expenses (including counsel fees).....	10,000.00
Printing expenses.....	100,000.00
Miscellaneous.....	121,492.03
	-----
Total.....	\$650,000.00
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## ITEM 15. INDEMNIFICATION OF DIRECTORS AND OFFICERS.

Article Seven of the Registrant's Restated Certificate of Incorporation requires indemnification of the Registrant's officers and directs that such indemnification be made to the fullest extent permitted by the New York Business Corporation Law.

Section 722 of the New York Business Corporation Law permits a corporation to provide for the indemnification of the members of its board of directors and its officers against actions or proceedings, or the threat thereof, by or in the right of the corporation. In order to receive indemnification, such director or officer must have (i) acted in good faith for a purpose which he reasonably believed was in the best interest of the corporation, and (ii) in the case of a criminal proceeding, also had no reasonable belief that such conduct was unlawful.

Article IV of the Company's By-Laws provides that the directors and certain other personnel of the Company shall be indemnified against expenses and certain other liabilities arising out of legal actions brought or threatened against them for their conduct on behalf of the Company, subject to certain qualifications and provided that each such person acted in good faith and in a manner that they reasonably believed was in the Company's best interest.

Each of the directors has entered into an agreement with the Company that provides that the Company will indemnify such director to the fullest extent permitted by the New York Business Corporation Law. The Company maintains directors' and officers' liability insurance which insures against liabilities that directors or officers of the Company may incur in such capacities.

Reference is made to the proposed Underwriting Agreement filed as Exhibit 1 to this Registration Statement for certain provisions relating to the indemnification of directors and officers of the Company against certain liabilities under the Securities Act of 1933.

## ITEM 16. EXHIBITS.

EXHIBIT NUMBER -----	DESCRIPTION -----
*1	-- Form of Underwriting Agreement.
4.1	-- Stock Purchase Agreement dated January 13, 1988, by and between the Company, Leonard S. Schleifer and ML Venture Partners II, L.P. (the "Stock Purchase Agreement"). Incorporated by reference to Exhibit 10.1 to Regeneron's Registration Statement on Form S-1 (File No. 33-39043) (the "Regeneron S-1").
4.2	-- Amendment to the Stock Purchase Agreement dated March 3, 1989. Incorporated by reference to Exhibit 10.2 to the Regeneron S-1.
4.3	-- Letter Agreement dated November 27, 1989, amending the Stock Purchase Agreement. Incorporated by reference to Exhibit 10.13 to the Regeneron S-1.
4.4	-- Class B Convertible Preferred Stock Purchase Agreement dated November 22, 1988, by and between the Company and each purchaser set forth on Exhibit A thereto. Incorporated by reference to Exhibit 10.3 to the Regeneron S-1.
4.5	-- Class D Convertible Preferred Stock Purchase Agreement dated August 31, 1990, by and between the Company and Amgen Inc. Incorporated by reference to Exhibit 10.9 to the Regeneron S-1.
4.6	-- Registration Rights Agreement, dated as of July 22, 1993, by and between the Company and Glaxo Group Limited. Incorporated by reference to Exhibit 4.7 to Regeneron's Registration Statement on Form S-3 (File No. 33-66788).
4.7	-- Registration Rights Agreement, dated as of April 15, 1996, by and between the Company and Amgen Inc. Incorporated by reference to Exhibit 10.3 to Regeneron's Form 10-Q for the quarter ended June 30, 1996, filed August 14, 1996.
4.8	-- Registration Rights Agreement, dated as of June 27, 1996, by and between the Company and Medtronic, Inc. Incorporated by reference to Exhibit 10.6 to Regeneron's Form 10-Q for the quarter ended June 30, 1996, filed August 14, 1996.
4.9	-- Registration Rights Agreement, dated as of December 11, 1996, by and between the Company and Procter & Gamble Pharmaceuticals. Incorporated by reference to Exhibit 10.30 to Regeneron's Form 10-K for the fiscal year ended December 31, 1996, filed March 26, 1997.
4.10	-- Registration Rights Agreement, dated as of May 13, 1997, by and between the Company and Procter & Gamble Pharmaceuticals. Incorporated by reference to Exhibit 10.3 to Regeneron's Form 10-Q for the quarter ended June 30, 1997, filed August 12, 1997.
4.11	-- Form of Certificate of shares of common stock. Incorporated by reference to Exhibit (a) to the Company's Form 8-A, filed with the Commission on February 20, 1991.
*5	-- Opinion of Skadden, Arps, Slate, Meagher & Flom LLP.
23.1	-- Consent of PricewaterhouseCoopers LLP, Independent Accountants.
23.2	-- Consent of Ernst & Young LLP, Independent Auditors.
*23.3	-- Consent of Skadden, Arps, Slate, Meagher & Flom LLP. Included in Exhibit 5.
24	-- Powers of Attorney. Included in the signature page of this Registration Statement.

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\* To be filed by amendment.

## ITEM 17. UNDERTAKINGS.

The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933 (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.

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 provisions described in "Item 14 -- Indemnification of Directors and Officers" above, or otherwise, the Registrant has been advised that in the opinion of the 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.

The undersigned Registrant hereby undertakes that:

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

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

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, 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 Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the Village of Tarrytown, State of New York on January 25, 2001.

REGENERON PHARMACEUTICALS, INC.

By: /s/ LEONARD S. SCHLEIFER, M.D., PH.D.

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Leonard S. Schleifer, M.D., Ph.D.  
President and Chief Executive  
Officer

PURSUANT TO THE REQUIREMENTS OF THE SECURITIES ACT OF 1933, THIS REGISTRATION STATEMENT HAS BEEN SIGNED BY THE FOLLOWING PERSONS IN THE CAPACITIES AND ON THE DATES INDICATED. EACH PERSON WHOSE SIGNATURE APPEARS BELOW HEREBY AUTHORIZES LEONARD S. SCHLEIFER, AND MURRAY A. GOLDBERG, JOINTLY AND SEVERALLY, WITH FULL POWER TO EACH, TO EXECUTE IN THE NAME AND ON BEHALF OF SUCH PERSON ANY AMENDMENT (INCLUDING ANY POST-EFFECTIVE AMENDMENTS) TO THIS REGISTRATION STATEMENT (OR ANY OTHER REGISTRATION STATEMENT FOR THE SAME OFFERING THAT IS TO BE EFFECTIVE UPON FILING PURSUANT TO RULE 462(B) UNDER THE SECURITIES ACT) AND TO FILE THE SAME, WITH EXHIBITS THERETO AND OTHER DOCUMENTS IN CONNECTION THEREWITH, MAKING SUCH CHANGES IN THIS REGISTRATION STATEMENT AS THE PERSON(S) SO ACTING DEEMS APPROPRIATE AND APPOINTS EACH OF SUCH PERSONS, EACH WITH FULL POWER OF SUBSTITUTION, ATTORNEY-IN-FACT TO SIGN ANY AMENDMENT (INCLUDING ANY POST-EFFECTIVE AMENDMENT) TO THIS REGISTRATION STATEMENT (OR ANY OTHER REGISTRATION STATEMENT FOR THE SAME OFFERING THAT IS TO BE EFFECTIVE UPON FILING PURSUANT TO RULE 462(B) UNDER THE SECURITIES ACT) AND TO FILE THE SAME, WITH EXHIBITS THERETO AND OTHER DOCUMENTS IN CONNECTION THEREIN.

SIGNATURE -----	TITLE -----	DATE -----
/s/ P. ROY VAGELOS, M.D. ----- P. Roy Vagelos, M.D.	Chairman of the Board	January 25, 2001
/s/ LEONARD S. SCHLEIFER, M.D., PH.D. ----- Leonard S. Schleifer, M.D., Ph.D	President, Chief Executive Officer and Director (Principal Executive Officer)	January 25, 2001
/s/ MURRAY A. GOLDBERG ----- Murray A. Goldberg	Senior Vice President, Finance & Administration, Chief Financial Officer, Treasurer, and Assistant Secretary (Principal Financial Officer)	January 25, 2001
/s/ DOUGLAS S. MCCORKLE ----- Douglas S. McCorkle	Controller and Assistant Treasurer (Principal Accounting Officer)	January 25, 2001

## SIGNATURE

## TITLE

## DATE

-----  
/s/ CHARLES A. BAKER

Director

January 25, 2001

-----  
Charles A. Baker

/s/ MICHAEL S. BROWN, M.D.

Director

January 25, 2001

-----  
Michael S. Brown, M.D.

/s/ ALFRED G. GILMAN, M.D., PH.D

Director

January 25, 2001

-----  
Alfred G. Gilman, M.D., Ph.D.

/s/ JOSEPH L. GOLDSTEIN, M.D.

Director

January 25, 2001

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Joseph L. Goldstein, M.D.

/s/ FRED A. MIDDLETON

Director

January 25, 2001

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Fred A. Middleton

/s/ ERIC M. SHOOTER, PH.D

Director

January 25, 2001

-----  
Eric M. Shooter, Ph.D.

/s/ GEORGE L. SING

Director

January 25, 2001

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George L. Sing

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*5	-- Opinion of Skadden, Arps, Slate, Meagher & Flom LLP.
23.1	-- Consent of PricewaterhouseCoopers LLP, Independent Accountants.
23.2	-- Consent of Ernst & Young LLP, Independent Auditors.
*23.3	-- Consent of Skadden, Arps, Slate, Meagher & Flom LLP. Included in Exhibit 5.
24	-- Powers of Attorney. Included in the signature page of this Registration Statement.

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\* To be filed by amendment.

## EXHIBIT 23.1

## CONSENT OF INDEPENDENT ACCOUNTANTS

We hereby consent to the incorporation by reference in this Registration Statement on Form S-3 of our report, which is based in part on the report of other auditors, dated February 8, 2000 relating to the financial statements, which appears in Regeneron Pharmaceuticals, Inc.'s Annual Report on Form 10-K for the year ended December 31, 1999. We also consent to the reference to us under the heading "Experts" in such Registration Statement.

PRICEWATERHOUSECOOPERS LLP

New York, New York  
January 25, 2001

## EXHIBIT 23.2

## CONSENT OF ERNST &amp; YOUNG LLP, INDEPENDENT AUDITORS

We consent to the reference to our firm under the caption "Experts" in the Registration Statement (Form S-3) and related Prospectus of Regeneron Pharmaceuticals, Inc. for the registration of 4,600,000 shares of its common stock and to the incorporation by reference therein of our report dated February 8, 2000, with respect to the financial statements of Amgen Regeneron Partners included in Regeneron Pharmaceuticals, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 1999, filed with the Securities and Exchange Commission.

ERNST & YOUNG LLP

Los Angeles, California  
January 25, 2001