REGENERON PHARMACEUTICALS INC
Form 10-K/A
March 19, 2004

Table of Contents

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K/A

Amendment No. 1

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2003

OR

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number 0-19034

REGENERON PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

New York	**13-3444607**
(State or other jurisdiction of incorporation or organization)	*(I.R.S. Employer Identification No)*
777 Old Saw Mill River Road, Tarrytown, New York	**10591-6707**
(Address of principal executive offices)	*(Zip code)*

(914) 347-7000

(Registrant s telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

None

(Title of Class)

Securities registered pursuant to Section 12(g) of the Act:

Common Stock par value $.001 per share

(Title of Class)

Preferred Share Purchase Rights expiring October 18, 2006

(Title of Class)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes þ No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Act). Yes þ No o

The aggregate market value of voting stock held by non-affiliates of the registrant as of June 30, 2003, was $546,128,000.

Indicate the number of shares outstanding of each of Registrant s classes of common stock as of February 29, 2004:

Class of Common Stock	Number of Shares
Class A Stock, $.001 par value	2,365,873
Common Stock, $.001 par value	53,197,081

DOCUMENTS INCORPORATED BY REFERENCE:

The Registrant s definitive proxy statement to be filed in connection with solicitation of proxies for its 2004 Annual Meeting of Shareholders is incorporated by reference into Part III of this Form 10-K. Exhibit index is located on pages 40 to 42 of this filing.

Table of Contents

EXPLANATORY NOTE:

This Amendment No. l to the Annual Report on Form 10-K for the fiscal year ended December 31, 2003 of Regeneron Pharmaceuticals, Inc. is being filed solely to conform the form of certifications included in Exhibit 31 previously filed with the Annual Report on Form 10-K to new Exchange Act Rule requirements. In all other respects, the text of this Amendment, including the financial statements filed as part of this report, remains unchanged from the previously filed Annual Report on Form 10-K.

TABLE OF CONTENTS

Table of Contents

PART I

Item 1. *Business*

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties relating to the future financial performance of Regeneron Pharmaceuticals, Inc. and actual events or results may differ materially. These statements concern, among other things, the possible success and therapeutic applications of our product candidates and research programs, the timing and nature of the clinical and research programs now underway or planned, and the future sources and uses of capital and our financial needs. These statements are made by us based on management s current beliefs and judgment. In evaluating such statements, stockholders and potential investors should specifically consider the various factors identified under the caption Risk Factors which could cause actual results to differ materially from those indicated by such forward-looking statements. We do not undertake any obligation to update publicly any forward-looking statement, whether as a result of new information, future events, or otherwise, except as required by law.

General

Regeneron Pharmaceuticals, Inc. is a biopharmaceutical company that discovers, develops, and intends to commercialize pharmaceutical products for the treatment of serious medical conditions. Our clinical and preclinical pipeline includes product candidates for the treatment of cancer, diseases of the eye, rheumatoid arthritis and other inflammatory conditions, allergies, asthma, obesity, and other diseases and disorders. Developing and commercializing new medicines entails significant risk and expense. Since inception we have not generated any sales or profits from the commercialization of any of our product candidates.

Our core business strategy is to combine our strong foundation in basic scientific research and discovery-enabling technology with our 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. We believe that our ability to develop product candidates is enhanced by the application of our technology platforms. These platforms are designed to discover specific genes of therapeutic interest for a particular disease or cell type and validate targets through high-throughput production of mammalian models. We continue to invest in the development of enabling technologies to assist in our efforts to identify, develop, and commercialize new product candidates.

Below is a summary of our clinical programs.

VEGF TRAP: Protein-based product candidate designed to bind Vascular Endothelial Growth Factor (called VEGF, also known as Vascular Permeability Factor or VPF) and its relative, Placental Growth Factor (called PLGF), and prevent their interaction with cell surface receptors. VEGF (and to a less validated degree PLGF) is required for the growth of blood vessels that are needed for tumors to grow and is a potent regulator of vascular permeability and leakage. In 2001, we initiated a dose-escalation Phase I clinical trial designed to assess the safety and tolerability of the VEGF Trap in subjects with advanced solid tumor malignancies. This trial continues to test increasing doses of VEGF Trap delivered by subcutaneous injection as per the protocol and is expected to be completed in the first half of 2004. A second phase, expected to begin in the first half of 2004, will test higher doses of the VEGF Trap delivered intravenously. We are also evaluating the VEGF Trap for the potential treatment of certain eye diseases and in March 2004, announced the initiation of a Phase I study of the VEGF Trap in patients with the neovascular or wet form of age-related macular degeneration.

In September 2003, we entered into a collaboration agreement with Aventis Pharmaceuticals Inc. to jointly develop and commercialize the VEGF Trap in multiple oncology, ophthalmology, and possibly other indications throughout the world with the exception of Japan, where product rights remain with us. Aventis made a non- refundable up-front payment of $80.0 million and purchased 2,799,552 newly issued unregistered shares of our Common Stock for $45.0 million. Under the collaboration agreement,

Table of Contents

we and Aventis will share co-promotion rights and profits on sales, if any, of the VEGF Trap. Aventis has agreed to make a $25.0 million payment to us upon achievement of an early-stage clinical milestone. We may also receive up to $360.0 million in additional milestone payments upon receipt of specified marketing approvals for up to eight VEGF Trap indications in Europe or the United States. Regeneron has agreed to continue to manufacture clinical supplies of the VEGF Trap at our plant in Rensselaer, New York. Aventis has agreed to be responsible for providing commercial scale manufacturing capacity for the VEGF Trap.

Under the collaboration agreement, agreed upon development expenses incurred by both companies during the term of the agreement will be funded by Aventis. If the collaboration becomes profitable, we will reimburse Aventis for 50% of the VEGF Trap development expenses in accordance with a formula based on the amount of development expenses and our share of the collaboration profits, or at a faster rate at our option. In 2004, we and Aventis plan to invest approximately $100 million to support the development of the VEGF Trap. The broad based development program will include multiple Phase I studies to evaluate the VEGF Trap in combination with other therapies in various cancer indications, Phase II single-agent studies of the VEGF Trap in separate cancer indications, and multiple Phase I studies of the VEGF Trap in certain eye diseases.

INTERLEUKIN-1 TRAP (IL-1 Trap): Protein-based product candidate designed to bind the interleukin-1 (called IL-1) cytokine and prevent its interaction with cell surface receptors. IL-1 is thought to play an important role in rheumatoid arthritis and other inflammatory diseases. In October 2003, we announced that the IL-1 Trap demonstrated evidence of clinical activity and safety in patients with rheumatoid arthritis (RA) in a Phase II dose-ranging study in approximately 200 patients. Patients treated with the highest dose, 100 milligrams of the IL-1 Trap, exhibited non-statistically significant improvements in the proportion of American College of Rheumatology (ACR) 20 responses versus placebo, the primary endpoint of the trial. Patients treated with the IL-1 Trap also exhibited improvements in secondary endpoints of the trial. The IL-1 Trap was generally well tolerated and was not associated with any drug-related serious adverse events.

On February 27, 2004, Regeneron announced plans to initiate a Phase IIb study of the IL-1 Trap in patients with rheumatoid arthritis in the second half of 2004. The Phase IIb study will be conducted in a larger patient population, testing higher doses and for a longer period of time than in the previous Phase II trial. In addition, we intend to conduct studies of the IL-1 Trap in a variety of other inflammatory diseases where interleukin-1 is believed to play a critical role. We are currently working on new product formulations that would allow delivery of higher doses of IL-1 Trap either through subcutaneous or intravenous administration and plan to conduct patient tolerability studies in the first half of 2004.

Since March 2003, we have been collaborating with Novartis Pharma AG on the development of the IL-1 Trap. On February 27, 2004, we announced that Novartis had provided notice of its intention not to proceed with the joint development of the IL-1 Trap. Under the terms of the collaboration agreement, Novartis remains obligated to fund agreed upon pre-Phase III IL-1 Trap development expenses during the nine-month notice period before its voluntary termination becomes effective. Novartis and we retain rights under the collaboration agreement to elect to collaborate on the development and commercialization of other IL-1 antagonists being developed independently by the other party that are in earlier stages of development than the IL-1 Trap.

INTERLEUKIN-4/ INTERLEUKIN-13 TRAP (IL-4/13 Trap): Protein-based product candidate designed to bind both the interleukin-4 and interleukin-13 (called IL-4 and IL-13) cytokines and prevent their interaction with cell surface receptors. IL-4 and IL-13 are thought to play a major role in diseases such as asthma, allergic disorders, and other inflammatory diseases. In October 2002, we initiated a Phase I trial for the IL-4/13 Trap in adult subjects with mild to moderate asthma. This placebo-controlled, double-blind, dose escalation study is designed to assess the safety and tolerability of the IL-4/13 Trap. The trial is expected to be completed in the first quarter of 2004 and we anticipate

Table of Contents

presenting the results at a scientific conference in the second quarter of 2004. We are also evaluating the potential use of the IL-4/13 Trap in other therapeutic indications.

AXOKINE®: Protein-based product candidate designed to act on the brain region regulating appetite and energy expenditure. AXOKINE is being developed for the treatment of obesity. In March 2003, we reported data from the 12-month treatment period of our initial Phase III pivotal trial of AXOKINE. The double-blind treatment period in this study is being followed by a twelve-month open-label extension phase, during which all study subjects receive AXOKINE. The extension phase is expected to be completed in the first quarter of 2004. We are currently conducting research on improving the formulation and delivery of AXOKINE and evaluating its commercial potential. We do not expect to initiate any Phase III clinical trials of AXOKINE in 2004.

Our Areas of Focus

Anti-Angiogenesis/Angiogenesis in Cancer and Other Settings: VEGF Trap and the Angiopoietins

Research. 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.

In many clinical settings, 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 the heart, aid in healing 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 was the first growth factor shown to be specific for blood vessels, by virtue of having its receptor specifically expressed on blood vessel cells. In 1994, we discovered a second family of angiogenic growth factors, termed the Angiopoietins, and we have received patents covering 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. The Angiopoietins are being evaluated in preclinical research by us and our academic collaborators.

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

The approach of inhibiting angiogenesis as a mechanism of action for an oncology medicine was further validated in February 2004, when the U.S. Food and Drug Administration (or FDA) approved Genentech, Inc. s VEGF inhibitor, Avastin . Avastin is an antibody product designed to inhibit VEGF and interfere with the blood supply to cancerous tumors. We exploited our Trap technology (which is described below) to develop a protein-based blocker of VEGF, referred to as the VEGF Trap.

Oncology. Cancer is a heterogeneous set of diseases and one of the leading causes of death in the developed world. A mutation in any one of dozens of normal genes can eventually lead a cell to become cancerous; however, a common feature of cancer cells is that they need to get nutrients and remove waste products, just as normal cells do. The vascular system is designed to supply nutrients and remove waste from normal tissues. Cancer cells can use the vascular system either by taking over preexisting blood vessels or by promoting the growth of new blood vessels. VEGF is secreted by many tumors to stimulate the growth of new

Table of Contents

blood vessels to support the tumor. Countering the effects of VEGF, thus blocking the blood supply to tumors, has been shown to provide therapeutic benefits.

Diseases of the Eye. Age-Related Macular Degeneration (AMD) and Diabetic Retinopathy (DR) are two of the leading causes of adult blindness in the developed world. In both conditions, severe visual loss is caused by a combination of retinal edema and neovascular proliferation. VEGF both stimulates angiogenesis and increases vascular permeability, has been shown to be a major pathogenic factor in both DR and AMD, and is believed to be involved in other medical problems affecting the eyes. Counteracting the effects of VEGF may provide a significant therapeutic benefit to patients suffering from these disorders.

AMD is a leading cause of severe visual loss in people over the age of 55 in developed countries. It is estimated that, in the U.S., 6% of individuals aged 65-74 and 20% of those older than 75 are affected with AMD. DR is a major complication of diabetes mellitus that can lead to significant vision impairment. DR is characterized, in part, by vascular leakage, which results in the collection of fluid in the retina. When the macula, the central area that is responsible for fine visual acuity, is involved, loss of visual acuity occurs. This is referred to as Diabetic Macular Edema (DME). DME is the most prevalent cause of moderate visual loss in patients with diabetes.

Clinical Development VEGF Trap. In November 2001, we initiated a Phase I clinical trial designed to assess the safety and tolerability of the VEGF Trap in subjects with solid tumor malignancies. The Phase I trial is an open-label study in subjects with advanced tumors and is evaluating the VEGF Trap at increasing dose levels. The ongoing study is being conducted at three clinical sites in the United States, and the trial is expected to be completed in the first half of 2004. A second phase, expected to begin in the first half of 2004, will test higher doses of the VEGF Trap delivered intravenously. We are also evaluating the VEGF Trap for the potential treatment of certain diseases of the eye and in March 2004, announced the initiation of a Phase I study of the VEGF Trap in patients with the neovascular or wet form of age-related macular degeneration.

In September 2003, we entered into a Collaboration Agreement with Aventis to jointly develop and commercialize the VEGF Trap in multiple oncology, ophthalmology, and possibly other indications throughout the world with the exception of Japan, where product rights remain with us. In 2004, we and Aventis plan to invest approximately $100 million to support the development of the VEGF Trap. The broad based development program will include multiple Phase I studies to evaluate the VEGF Trap in combination with other therapies in various cancer indications, Phase II single-agent studies of the VEGF Trap in separate cancer indications, and multiple Phase I studies of the VEGF Trap in certain eye diseases.

Trap Technology and Additional Traps

Research. Our research on ciliary neurotrophic factor, or CNTF, led to the discovery that CNTF, although it is a neurotrophic factor, belongs to the superfamily of signaling molecules called 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 medicines or product candidates already approved or in clinical development. The cytokine superfamily includes factors such as erythropoietin, thrombopoietin, granulocyte-colony stimulating factor, and the interleukins (or ILs).

During the 1990s, our scientists made a number of breakthroughs in understanding how receptors work for an entire family of cytokines, which had broad relevance for many other families of cytokines and growth factors. Based on these findings, we developed a new class of protein-based antagonists, termed Traps, which could be designed to target and block specific cytokines and growth factors implicated in human disease. Examples include the VEGF Trap (designed to block VEGF and PLGF), the IL-1 Trap (designed to block both IL-1 alpha and IL-1 beta), the IL-4 Trap (designed to block IL-4), the IL-6 Trap (designed to block IL-6), the IL-18 Trap (designed to block IL-18), and the IL-4/13 Trap (designed to block IL-4 and IL-13).

Table of Contents

In preclinical studies, these Traps are more potent than other growth factor and cytokine antagonists, potentially allowing lower levels of these drug candidates to be used. Moreover, because these Traps are comprised entirely of natural human-derived protein sequences, they may be less likely to induce an immune reaction in humans. Because pathological levels of certain cytokines and growth factors seem to contribute to a variety of diseases, our Traps have the potential to be important therapeutic agents.

We have clinical programs underway for our IL-1 Trap and IL-4/13 Trap (see below) and research programs underway for an IL-6 Trap and an IL-18 Trap. 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. IL-18 is thought to contribute to a number of inflammatory and immunological diseases and disorders. We also have patents covering additional Traps for IL-2, IL-3, IL-5, IL-15, and others, which are being studied in earlier stage research programs. Our research also includes molecular and cellular research to improve or modify 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 Traps.

Clinical Development.

IL-1 Trap. 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 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 roughly two-thirds of these patients.

In July 2002, we announced the initiation of a dose-ranging Phase II study of the IL-1 Trap in subjects with rheumatoid arthritis. This trial enrolled approximately 200 subjects who received weekly self-injections of one of three fixed doses of IL-1 Trap or placebo for 12 weeks, followed by 10 weeks of off-treatment follow-up. In October 2003, we announced that in this trial the IL-1 Trap demonstrated evidence of clinical activity and safety. Patients treated with the highest dose, 100 milligrams of the IL-1 Trap, exhibited non-statistically significant improvements in the proportion of American College of Rheumatology (ACR) 20 responses versus placebo, the primary endpoint of the trial. Patients treated with the IL-1 Trap also exhibited improvements in secondary endpoints of the trial. The IL-1 Trap was generally well tolerated and was not associated with any drug-related serious adverse events.

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IL-4/13 Trap. 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 a fast 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,

Table of Contents

however, it is thought that excess levels of IL-4 and IL-13 causes overactivity of the immune system, which contributes to disease initiation and progression.

Antagonists for IL-4 and IL-13 may be therapeutically useful in a number of allergy and asthma-related conditions, including as an adjunct to vaccines where blocking IL-4 and IL-13 may help to elicit more of the desired type of immune response to the vaccine. We have developed both an IL-4 Trap and an IL-4/13 Trap, which is a single molecule that can block both interleukin-4 and interleukin-13. In October 2002, we initiated a placebo-controlled, double-blind, dose escalation Phase I clinical trial designed to assess the safety and tolerability of the IL-4/13 Trap in subjects with mild to moderate asthma. The trial is expected to be completed in the first quarter of 2004. We are also evaluating the potential use of the IL-4/13 Trap in other therapeutic indications.

Obesity and Metabolic Diseases

Food intake and metabolism are regulated by complex interactions between diverse neural and hormonal signals that serve to maintain an optimal balance between energy intake, storage, and utilization. The hypothalamus, a small area at the base of the brain, is critically involved in the integration of peripheral signals which reflect nutritional status and neural outputs which regulate appetite, food seeking behaviors, and energy expenditure. Obesity and related metabolic disorders, such as type 2 diabetes, reflect a dysregulation in the systems which ordinarily tightly couple energy intake to energy expenditure. Our preclinical research program encompasses the study of both central (neuropeptide) and peripheral (hormonal) regulators of food intake and metabolism in health and disease.

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 2 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. Several studies published in 2002 demonstrate that even modest levels of weight loss, when maintained over an extended period of time, can significantly reduce the risk of developing type 2 diabetes. 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 medicines. There are several approved medicines currently indicated for the treatment of obesity, including sibutramine (Meridia®, a registered trademark of Abbott Laboratories) and orlistat (Xenical®, a registered trademark of Hoffmann-LaRoche, Inc.).

Clinical Development AXOKINE. We are developing AXOKINE for the treatment of obesity. AXOKINE is our patented genetically re-engineered form of CNTF. In March 2003, we reported data from the 12-month treatment period of our initial Phase III pivotal trial of AXOKINE. The double-blind treatment period in this study is being followed by a twelve-month open-label extension phase, during which all study subjects receive AXOKINE. The extension phase is expected to be completed in the first quarter of 2004.

Two AXOKINE trials remain ongoing. These trials, which each include approximately 300 subjects, are evaluating the safety of intermittent treatment with AXOKINE and studying maintenance of weight loss following short-term treatment regimens. Results from these trials are expected to be available in mid-2004.

We are currently conducting research on improving the formulation and delivery of AXOKINE and evaluating its commercial potential. We do not expect to initiate any Phase III clinical trials of AXOKINE in 2004.

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 treat subjects with muscle atrophy or other muscle conditions which afflict millions of people globally. Thus, a

Table of Contents

treatment that has 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 pathways involved in muscle atrophy and hypertrophy, and discovering therapeutic candidates that can modulate these pathways. This work is being conducted in collaboration with scientists at The Procter & Gamble Company.

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). We have also demonstrated that this growth factor receptor system is required for normal cartilage development in mice. In addition, together with collaborators, we have demonstrated 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, but we have not yet identified any therapeutic molecules from our research to advance to clinical development.

Fibrosis

Fibrotic diseases, such as cirrhosis, result from the excess production of fibrous extracellular matrix by certain cell types. 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. Our work in this area is currently focused on determining whether selective inhibition or activation of DDR1 and DDR2 would be beneficial in the setting of fibrotic disease. Further, we are studying key signaling pathways which allow particular fibrosis-inducing cells to multiply. Inhibition of such pathways may be useful in preventing the development of fibrosis. These research activities are being conducted in collaboration with scientists at Procter & Gamble.

G-Protein Coupled Receptors

G-Protein Coupled Receptors have historically been among the most useful targets for pharmaceuticals. We use a genomics approach to discover new G-Protein Coupled Receptors and then we characterize these receptors in our disease models by examining their expression. Early stage research work on selected G-Protein Coupled Receptors is being conducted in collaboration with scientists at Procter & Gamble.

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, direct licensing or sale of technology, or the establishment of research collaborations to discover and develop drug targets. In December 2002, we entered into an agreement with Serono S.A. to use excess capacity from our Velocigene technology platform to provide Serono with knock-out and transgenic mammalian models of gene function. Under the agreement, which was amended as of January 1, 2004 to expand the scope of services available under the Velocigene platform, Serono will pay us up to $4.0 million annually for up to five years.

Targeted Genomics . 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 the Angiopoietin and Ephrin growth factor families for angiogenesis and vascular disorders, the MuSK growth

Table of Contents

factor receptor system for muscle disorders, and the Regeneron Orphan Receptor (ROR) growth factor receptor system that regulates cartilage formation.

Velocigene. A major challenge facing the biopharmaceutical industry in the post-genomic era is 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 mammalian models in which the gene is removed (referred to as knock-out mammalian models), or is over-produced (referred to as transgenic mammalian models), or in which a color-producing gene is substituted for the gene of interest (referred to as reporter knock-in mammalian models) to identify which cells in the model system are expressing the gene. Until recently, technical hurdles involved in the generation of mammalian models restricted the ability to produce multiple models quickly and efficiently. We have developed proprietary technology that allows for the rapid and efficient production of models on a high throughput scale, enabling rapid assignment of function to gene sequences.

Designer Protein Therapeutics. 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. This technology platform has already produced more than 10 patented proteins, including the VEGF Trap and the IL-1 Trap, which are currently in clinical testing, and several others in preclinical development.

Our Collaborative Programs

We have entered into collaboration and licensing agreements with various companies, including Aventis, Novartis, Procter & Gamble, Amgen Inc., Sumitomo Chemical Company, Ltd., Medarex, Inc., Emisphere Technologies, Inc., and Nektar Therapeutics. In addition, we conduct many research programs in collaboration with academic partners. In the future, we may enter into additional strategic collaborations or licensing agreements focusing on one or more of our product candidates, research programs, or technology platforms. Below are summaries of our major collaborations.

Aventis. In September 2003, we entered into a collaboration agreement with Aventis to jointly develop and commercialize the VEGF Trap. Aventis made a non-refundable up-front payment of $80.0 million and purchased 2,799,552 newly issued unregistered shares of our Common Stock for $45.0 million.

Under the collaboration agreement, we and Aventis will share co-promotion rights and profits on sales, if any, of the VEGF Trap. Aventis has agreed to make a $25.0 million payment to us upon achievement of an early-stage clinical milestone. We may also receive up to $360.0 million in additional milestone payments upon receipt of specified marketing approvals for up to eight VEGF Trap indications in Europe or the United States. Regeneron has agreed to continue to manufacture clinical supplies of the VEGF Trap at our plant in Rensselaer, New York. Aventis has agreed to be responsible for providing commercial scale manufacturing capacity for the VEGF Trap.

Under the collaboration agreement, agreed upon development expenses incurred by both companies during the term of the agreement will be funded by Aventis. If the collaboration becomes profitable, we will reimburse Aventis for 50 percent of the VEGF Trap development expenses in accordance with a formula based on the amount of development expenses and our share of the collaboration profits, or at a faster rate at our option.

Aventis has the right to terminate the agreement without cause with at least twelve months advance notice. Upon termination of the agreement for any reason, any remaining obligation to reimburse Aventis for 50 percent of the VEGF Trap development expenses will also terminate and we will retain all rights to the VEGF Trap.

Novartis. In March 2003, we entered into a collaboration agreement with Novartis to jointly develop and commercialize the IL-1 Trap. Novartis made a non-refundable up-front payment of $27.0 million and purchased 7,527,050 newly issued unregistered shares of our common stock for $48.0 million.

Table of Contents

Development expenses incurred during 2003 were shared equally by us and Novartis. We funded our share of 2003 expenses through a loan from Novartis that will be forgiven, together with accrued interest, should certain preclinical and clinical milestones be reached, and is otherwise due and payable on July 1, 2004.

On February 27, 2004, we announced that Novartis had provided notice of its intention not to proceed with the joint development of the IL-1 Trap. Under the terms of the collaboration agreement, Novartis remains obligated to fund agreed upon pre-Phase III IL-1 Trap development expenses during the nine-month notice period before its voluntary termination becomes effective. Novartis and we retain rights under the collaboration agreement to elect to collaborate on the development and commercialization of other IL-1 antagonists being developed independently by the other party that are in earlier stages of development than the IL-1 Trap.

Procter & Gamble. In May 1997, we entered into a long-term collaboration agreement with Procter & Gamble to discover, develop, and commercialize pharmaceutical products. In connection with the collaboration, Procter & Gamble made equity purchases of our Common Stock of $42.9 million in June 1997 and $17.1 million 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 to provide funding in support of our research efforts related to the collaboration, of which we received $80.0 million through December 31, 2003. From 1997 to 1999, Procter & Gamble also provided research support for our AXOKINE program. As a result, Procter & Gamble will be entitled to receive a small royalty on any sales of AXOKINE.

In August 2000, Procter & Gamble made two non-recurring research progress payments to us totaling $3.5 million. Effective December 31, 2000, we and Procter & Gamble entered into a new long-term collaboration agreement, replacing the companies 1997 agreement. The new agreement extended 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 focused the companies collaborative research on therapeutic areas that are of particular interest to Procter & Gamble, including muscle atrophy and muscle diseases, fibrotic diseases, and selected G-Protein Coupled Receptors. For each of these program areas, the parties contribute research activities and necessary intellectual property rights pursuant to mutually agreed upon plans and budgets established by operating committees. During the first five years of the agreement, neither party may independently perform research on targets included in the collaboration.

We and Procter & Gamble divided rights to the programs from the 1997 collaboration agreement that are no longer part of the companies collaboration. Procter & Gamble obtained rights to certain early stage programs. We have rights to all other research programs including exclusive rights to the VEGF Trap, the Angiopoietins, and our Orphan Receptors (RORs). Any product candidates 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 new agreement, beginning in the first quarter of 2001, research support from Procter & Gamble is $2.5 million per quarter (before adjustments for inflation) through December 2005.

The new collaboration agreement expires on the later of December 31, 2005 or the termination of research, development, or commercial activities relating to compounds that meet predefined success criteria before that date. In addition, if either party successfully develops a compound covered under the agreement to a predefined development stage during the two-year period following December 31, 2005, the parties shall meet to determine whether to reconvene joint development of the compound under the agreement. The agreement is also subject to termination if either party enters bankruptcy, breaches its material obligations, or undergoes a change of control. In addition to 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 generally does 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.

Table of Contents

Manufacturing

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

In 1993, we purchased our 104,000 square foot Rensselaer, New York manufacturing facility, and in 2003 completed a 19,500 square foot expansion. This facility is used to manufacture therapeutic candidates for our own preclinical and clinical studies. We also use the facility to manufacture a product for Merck & Co., Inc. under a contract that expires in 2005. In July 2002, we leased 75,000 square feet in a building near our Rensselaer facility which is being used for the manufacture of Traps and for warehouse space. As of December 31, 2003, there were no impairment losses associated with long-lived assets.

At December 31, 2003, we employed 274 people in our manufacturing operations at these facilities.

In 1995, we entered into a long-term manufacturing agreement with Merck (called, as amended, the Merck Agreement) to produce an intermediate for a Merck pediatric vaccine at our Rensselaer facility. We agreed to modify portions of our facility for manufacture of the Merck intermediate and to assist Merck in securing regulatory approval for manufacturing in the Rensselaer facility. In December 1999, we announced that the FDA had approved us as a contract manufacturer for the Merck intermediate. Under the Merck Agreement, we are manufacturing intermediate for Merck for six years, with certain minimum order quantities each year. The Merck Agreement extends through 2005, but may be terminated at any time by Merck upon one year s notice and may be extended by mutual agreement. Merck reimbursed us for the capital costs to modify the facility and for the cost of our activities performed on behalf of Merck prior to the start of production. Merck pays an annual facility fee of $1.0 million, subject to annual adjustment for inflation, reimburses us for certain manufacturing costs, pays us a variable fee based on the quantity of intermediate supplied to Merck, and makes certain additional payments. We recognized contract manufacturing revenue related to the Merck Agreement of $10.1 million in 2003, $11.1 million in 2002, and $9.8 million in 2001.

Among the conditions for regulatory marketing approval of a medicine is the requirement that the prospective manufacturer s quality control and manufacturing procedures conform to the GMP regulations of the health authority. In complying with standards set forth in these regulations, manufacturers must continue to expend time, money, and effort in the area of production and quality control to ensure full technical compliance. Manufacturing establishments, both foreign and domestic, are also subject to inspections by or under the authority of the FDA and by other national, federal, state, and local agencies. 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.

Competition

There is substantial competition in the biotechnology and pharmaceutical industries from pharmaceutical, biotechnology, and chemical companies. Our competitors may include Genentech, Novartis, Pfizer Inc., Hoffmann-LaRoche, Abbott Laboratories, Sanofi-Synthelabo, Merck, Amgen, and others. 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. 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. 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.

VEGF Trap. Many companies are developing therapeutic molecules designed to block the actions of VEGF specifically and angiogenesis in general. A variety of approaches have been employed, including

Table of Contents

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 molecules may be at a more advanced stage of development than our product candidate. In particular, Genentech recently was granted approval by the FDA to market and sell Avastin , a monoclonal antibody to VEGF. The marketing approval for Avastin may make it more difficult for us to enroll patients in clinical trials to support the VEGF Trap. This may delay or impair our ability to successfully develop and commercialize the VEGF Trap. In addition, Eyetech Pharmaceuticals, Inc. has successfully advanced its clinical candidate for eye diseases, Macugen, through Phase II/III trials. Eyetech is collaborating with Pfizer to develop and commercialize Macugen. If they receive approval to market Macugen for eye diseases, it would be more difficult for us to enroll patients in clinical trials for the VEGF Trap in eye diseases. This may delay or impair our ability to successfully develop and commercialize the VEGF Trap.

Cytokine Traps. Marketed products for the treatment of rheumatoid arthritis and asthma are available as either oral or inhaled medicines, 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 medicines are available for these diseases. Examples include the TNF-antagonists Enbrel® (a registered trademark of Amgen), Remicade® (a registered trademark of Centocor), and Humira® (a registered trademark of Abbott) for rheumatoid arthritis, and the leukotriene-modifier Singulair® (a registered trademark of Merck), as well as various inexpensive corticosteroid medicines for asthma. The availability of highly effective FDA approved TNF-antagonists makes it more difficult to successfully develop the IL-1 Trap for the treatment of rheumatoid arthritis. It will be difficult to enroll patients with rheumatoid arthritis to participate in clinical trials of the IL-1 Trap, which may delay or impair our ability to successfully develop the drug candidate. In addition, even if the IL-1 Trap is ever approved for sale, it will be difficult for our drug to compete against these FDA approved TNF-antagonists because doctors and patients will have significant experience using these effective medicines.

AXOKINE. There is substantial competition in the discovery and development of treatments for obesity, as well as established, cost-effective, and emerging prescription and over-the-counter treatments for this condition. For example, Hoffmann-LaRoche and Abbott already market well-established medicines for the treatment of obesity and Amgen, Sanofi-Synthelabo, and a number of other pharmaceutical companies are developing new potential therapeutics. Sanofi-Synthelabo has a cannaboid receptor antagonist in Phase III clinical development. In March 2004, Sanofi-Synthelabo reported that patients treated with this clinical candidate demonstrated significant weight loss in completed Phase III clinical trials. Many of these medicines or therapeutic candidates appear to offer competitive advantages over AXOKINE. For example, AXOKINE currently is available only in injectible form, while the currently available marketed medicines for the treatment of obesity and Sanofi-Synthelabo s product candidate are delivered in pill (or oral dosage) forms, which generally are favored by people over injectible medicines. 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.

Other Areas. 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. 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.

Table of Contents

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.

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 we consider important to the development of our business. We have been granted approximately 100 U.S. patents and we have approximately 100 pending U.S. applications. We are the 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 AXOKINE, Cytokine Traps, VEGF Trap, and Angiopoietins, as well as 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 July 2002, we announced that Amgen and Immunex Corporation (now part of Amgen) granted us a non-exclusive license to certain patents and patent applications which may be used in the development and commercialization of the IL-1 Trap. The license followed two other licensing arrangements under which we obtained a non-exclusive license to patents owned by ZymoGenetics, Inc. and Tularik Inc. for use in connection with the IL-1 Trap program. These license agreements would require us to pay royalties based on the net sales of the IL-1 Trap if and when it is approved for sale. In total, the royalty rate under these three agreements would be in the mid-single digits.

In August 2003, Merck granted us a non-exclusive license to certain patents and patent applications which may be used in the development and commercialization of AXOKINE. In consideration for the license, we issued to Merck 109,450 newly issued unregistered shares of our Common Stock and agreed to make an additional payment to Merck if the fair market value of the shares falls below a certain threshold at the time that Merck has the right to sell them. We agreed to make an additional payment upon receipt of marketing approval for a product covered by the licensed patents and pay royalties, at staggered rates in the mid-single digits, based on the net sales, if any, of products covered by the licensed patents.

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 may not file any such applications or, if filed, the patents may not be issued. Patents issued to or licensed by us may be infringed by the products or processes of others.

Defense and enforcement of our intellectual property 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

Table of Contents

have to alter or discontinue the development of our products or pay licensing fees to take into account patent rights of third parties.

Government Regulation

Regulation by government authorities in the United States and foreign countries is a significant factor in the research, development, manufacture, and marketing of our product candidates. All of our product candidates will require regulatory approval before they can be commercialized. In particular, human therapeutic products are subject to rigorous preclinical and clinical trials and other pre-market approval requirements by the FDA and foreign authorities. Many aspects of the structure and substance of the FDA and foreign pharmaceutical regulatory practices have been reformed during recent years, and continued reform is under consideration in a number of forums. The ultimate outcome and impact of such reforms and potential reforms cannot be predicted.

The activities required before a product candidate may be marketed in the United States begin with preclinical tests. Preclinical tests include laboratory evaluations and animal studies to assess the potential safety and efficacy of the product candidate and its formulations. The results of these studies must be submitted to the FDA as part of an Investigational New Drug Application, which must be reviewed by the FDA before proposed clinical testing can begin. Typically, clinical testing involves a three-phase process. In Phase I, trials are conducted with a small number of subjects to determine the early safety profile of the product candidate. In Phase II, clinical trials are conducted with subjects afflicted with a specific disease or disorder to provide enough data to evaluate the preliminary safety, tolerability, and efficacy of different potential doses of the product candidate. In Phase III, large-scale clinical trials are conducted with patients afflicted with the specific disease or disorder in order to provide enough data to understand the efficacy and safety profile of the product candidate, as required by the FDA. The results of the preclinical and clinical testing of a biologic product candidate are then submitted to the FDA in the form of a Biologics License Application, or BLA, for evaluation to determine whether the product candidate may be approved for commercial sale. In responding to a BLA, the FDA may grant marketing approval, request additional information, or deny the application.

Any approval required by the FDA for any of our product candidates may not be obtained on a timely basis, or at all. The designation of a clinical trial as being of a particular phase is not necessarily indicative that such a trial will be sufficient to satisfy the parameters of a particular phase, and a clinical trial may contain elements of more than one phase notwithstanding the designation of the trial as being of a particular phase. The results of preclinical studies or early stage clinical trials may not predict long-term safety or efficacy of our compounds when they are tested or used more broadly in humans.

Various federal and state statutes and regulations also govern or influence the research, manufacture, safety, labeling, storage, record keeping, marketing, transport, or other aspects of such product candidates. The lengthy process of seeking these approvals and the compliance with applicable statutes and regulations require the expenditure of substantial resources. Any failure by us or our collaborators or licensees to obtain, or any delay in obtaining, regulatory approvals could adversely affect the manufacturing or marketing of our products and our ability to receive product or royalty revenue.

In addition to the foregoing, our present and future business will be subject to regulation under the United States Atomic Energy Act, the Clean Air Act, the Clean Water Act, the Comprehensive Environmental Response, Compensation and Liability Act, the National Environmental Policy Act, the Toxic Substances Control Act, the Resource Conservation and Recovery Act, national restrictions, and other present and potential future local, state, federal, and foreign regulations.

Employees

As of December 31, 2003, we had 644 full-time employees, of whom 110 held 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; however, competition for these personnel is intense. None of our personnel are

Table of Contents

covered by collective bargaining agreements and our management considers its relations with our employees to be good.

Available Information

We file annual, quarterly, and current reports, proxy statements, and other documents with the Securities and Exchange Commission, or SEC, under the Securities Exchange Act of 1934, or the Exchange Act. The public may read and copy any materials that we file with the SEC at the SEC s Public Reference Room at 450 Fifth Street, NW, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. Also, the SEC maintains an Internet website that contains reports, proxy and information statements, and other information regarding issuers, including Regeneron, that file electronically with the SEC. The public can obtain any documents that we file with the SEC at *http://www.sec.gov*.

We also intend to make available free of charge on or through our Internet website *(http://www.regn.com)* our Annual Report on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and, if applicable, amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, as soon as reasonably practicable after we electronically file such material with, or furnish it to, the SEC.

Item 2. ***Properties***

We conduct our research, development, manufacturing, and administrative activities at our owned and leased facilities. We currently lease approximately 220,000 square feet, and sublease approximately 16,000 square feet, of laboratory, office, and manufacturing space in Tarrytown, New York. The sublease will convert to a direct lease with the landlord on December 31, 2005. We own a facility in Rensselaer, New York, consisting of two buildings totaling approximately 123,500 square feet of research, manufacturing, office, and warehouse space. We also lease an additional 75,000 square feet of manufacturing, office, and warehouse space in Rensselaer.

The following table summarizes the information regarding our current property leases:

Location	Square Footage	Expiration	Current Monthly Base Rental Charges(1)	Renewal Option Available
Tarrytown	146,000	December 31, 2007	$243,000	none
Tarrytown	16,000	December 31, 2007	$ 25,000	none
Tarrytown	74,000	December 31, 2009	$148,000	one 5-year term
Rensselaer	75,000	July 11, 2007	$ 23,000	two 5-year terms

(1) Excludes additional rental charges for utilities, taxes, and operating expenses, as defined.

In the future, we may lease, operate, or purchase additional facilities in which to conduct expanded research and development activities and manufacturing and commercial operations.

Item 3. ***Legal Proceedings***

In May 2003, securities class action lawsuits were commenced against Regeneron and certain of its officers and directors in the United States District Court for the Southern District of New York. A consolidated amended class action complaint was filed in October 2003. The complaint, which purports to be brought on behalf of a class consisting of investors in our publicly traded securities between March 28, 2000 and March 30, 2003, alleges that the defendants misstated or omitted material information concerning the safety and efficacy of AXOKINE, in violation of Sections 10(b) and 20(a) of the Securities and Exchange Act of 1934, and Rule 10b-5 promulgated thereunder. Damages are sought in an unspecified amount. We believe that the lawsuit is without merit and, in December 2003, we filed a motion to dismiss the lawsuit. Because we do not believe that a loss is probable, no legal reserve has been established.

Table of Contents

From time to time we are a party to other legal proceedings in the course of our business. Currently, we do not expect any other legal proceedings to have a material adverse effect on our business or financial condition.

Item 4. ***Submission of Matters to a Vote of Security Holders***

None.

Executive Officers of the Registrant

Listed below are our executive officers as of February 29, 2004. There are no family relationships between any of the executive officers and there is no arrangement or understanding between any executive officer and any other person pursuant to which the executive officer was selected. At the annual meeting of the Board of Directors, which follows the Annual Meeting of Shareholders, executive officers are elected by the Board to hold office for one year and until their respective successors are elected and qualified, or until their earlier resignation or removal.

Name	Age	Position
Leonard S. Schleifer, M.D., Ph.D.	51	President, Chief Executive Officer, and Founder
George D. Yancopoulos, M.D., Ph.D.	44	Executive Vice President and Chief Scientific Officer, and President, Regeneron Research Laboratories
Murray A. Goldberg	59	Senior Vice President, Finance & Administration, Chief Financial Officer, Treasurer, and Assistant Secretary
Randall G. Rupp, Ph.D.	56	Senior Vice President, Manufacturing Operations
Neil Stahl, Ph.D.	47	Senior Vice President, Preclinical Development and Biomolecular Science

Table of Contents

PART II

Item 5. ***Market for Registrant s Common Equity and Related Stockholder Matters***

Our Common Stock is quoted on The Nasdaq Stock Market under the symbol REGN. Our Class A Stock, par value $.001 per share, is not publicly quoted or traded.

The following table sets forth, for the periods indicated, the range of high and low sales prices for the Common Stock as reported by The Nasdaq Stock Market.

	High	Low
2002		
First Quarter	$30.20	$19.74
Second Quarter	25.40	12.21
Third Quarter	18.34	11.25
Fourth Quarter	22.85	12.25
2003		
First Quarter	$21.49	$ 7.40
Second Quarter	18.78	5.77
Third Quarter	22.35	12.22
Fourth Quarter	18.72	11.80

As of March 3, 2004, there were 635 shareholders of record of our Common Stock and 56 shareholders of record of our Class A Stock. The closing bid price for the Common Stock on that date was $15.00.

We have never paid cash dividends and do not anticipate paying any in the foreseeable future.

The information called for with respect to equity compensation plans is incorporated by reference to the material captioned Equity Compensation Plan Information in our definitive proxy statement with respect to our 2004 Annual Meeting of Shareholders to be filed with the SEC.

In March 2003, we entered into a collaboration agreement with Novartis to jointly develop and commercialize the IL-1 Trap. In connection with this agreement, we sold to Novartis 7,527,050 newly issued unregistered shares of our Common Stock for a purchase price of $48.0 million. We expect to use the proceeds from the sale of the Common Stock to fund working capital and general corporate purposes.

In August 2003, Merck granted us a non-exclusive license to certain patents and patent applications which may be used in the development and commercialization of AXOKINE. As consideration for this license, we issued to Merck 109,450 newly issued unregistered shares of our Common Stock.

In September 2003, we entered into a collaboration agreement with Aventis to jointly develop and commercialize the VEGF Trap. In connection with this agreement, we sold to Aventis 2,799,552 newly issued unregistered shares of our Common Stock for a purchase price of $45.0 million. We expect to use the proceeds from the sale of the Common Stock to fund working capital and general corporate purposes.

We view each of the aforementioned issuances as transactions not involving any public offering and therefore as exempt from registration under Section 4(2) of the Securities Act of 1933.

Table of Contents

Item 6. ***Selected Financial Data***

The selected financial data set forth below for the years ended December 31, 2003, 2002, and 2001 and at December 31, 2003 and 2002 are derived from and should be read in conjunction with our audited financial statements, including the notes thereto, included elsewhere in this report. The selected financial data for the years ended December 31, 2000 and 1999 and at December 31, 2001, 2000, and 1999 are derived from our audited financial statements not included in this report.

	Year Ended December 31,				
	2003	2002	2001	2000	1999
	(In thousands, except per share data)				
Statement of Operations Data					
Revenues					
Contract research and development	$ 47,366	$ 10,924	$12,071	$36,478	$24,539
Research progress payments				6,200	
Contract manufacturing	10,131	11,064	9,902	16,598	9,960
	57,497	21,988	21,973	59,276	34,499
Expenses					
Research and development(1)	136,024	124,953	92,542	65,134	52,450