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UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

(Mark One)

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

For the fiscal year ended December 31, 2004

OR

☐ **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 ☑ No ☐

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. ☐

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

The aggregate market value of voting stock held by non-affiliates of the registrant as of June 30, 2004, was $398,715,000.

Indicate the number of shares outstanding of each of Registrant's classes of common stock as of February 28, 2005:

Class of Common Stock	Number of Shares
Class A Stock, $.001 par value	2,358,373
Common Stock, $.001 par value	53,763,234

DOCUMENTS INCORPORATED BY REFERENCE:

Specified portions of the Registrant's definitive proxy statement to be filed in connection with solicitation of proxies for its 2005 Annual Meeting of Shareholders are incorporated by reference into Part III of this Form 10-K. Exhibit index is located on pages 44 to 47 of this filing.

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PART I

Item 1. *Business*

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties relating to future events and 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 events or 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, 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 pipeline of product candidates that we believe has the potential to address a variety of serious medical conditions. 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.

Here is a summary of the clinical status of our clinical candidates as of December 31, 2004:

- **VEGF TRAP — Oncology:** Protein-based product candidate designed to bind Vascular Endothelial Growth Factor (called VEGF, also known as Vascular Permeability Factor or VPF) and the related 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 new 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 1 clinical trial designed to assess the safety and tolerability of the VEGF Trap in subjects with advanced solid tumor malignancies. The preliminary results of this study were announced at the annual meeting of the American Society of Clinical Oncology (ASCO) in June 2004 and we updated these results in a poster session at the 16th Annual EORTC-NCI-AACR Symposium on Molecular Targets and Cancer Therapeutics in September 2004. The phase 1 trial was an open label, dose-escalation study conducted at three sites in the United States. The study enrolled and treated 38 patients with incurable, relapsed, or refractory solid tumors with subcutaneous injections of VEGF Trap. In total, the trial enrolled patients with 15 different types of cancer. Preliminary results of this study indicated that:
  - the VEGF Trap was generally well-tolerated at the dose levels studied, and
  - circulating levels of the VEGF Trap at the highest dose (1.6 milligrams per kilogram of body weight (mg/kg) per week) were consistent with levels observed to be effective in preclinical models.

Detailed results of the trial are expected to be submitted for publication in a peer-reviewed journal once all patients complete the extended treatment phase available to patients who maintained stable disease after the initial 10-week treatment period and the full results of the extension phase have been analyzed.

A second phase 1 trial, which commenced in April 2004, is studying higher VEGF Trap exposures through intravenous administration. This study is also designed to evaluate the safety, tolerability, and pharmacokinetics of intravenous VEGF Trap in advanced cancer patients.

We and the sanofi-aventis Group plan to initiate multiple clinical studies in 2005 to evaluate the VEGF Trap as a single-agent and in combination with other therapies in various cancer indications. During the third quarter of 2004, the U.S. Food and Drug Administration (FDA) granted Fast Track designation to the VEGF Trap for a specific niche cancer indication. As a result of the FDA's decision, we and sanofi–aventis plan to initiate a clinical trial in that indication in 2005.

In September 2003, we entered into a collaboration agreement with Aventis Pharmaceuticals, Inc. (now part of the sanofi-aventis Group) to jointly develop and commercialize the VEGF Trap throughout the world with the exception of Japan, where product rights remain with us. Under the collaboration agreement, as amended in January 2005, we and sanofi-aventis will share co-promotion rights and profits on sales, if any, of the VEGF Trap for disease indications included in our collaboration. In December 2004, we earned a $25.0 million payment from sanofi-aventis, which was received in January 2005, upon the 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.

Under the collaboration agreement, agreed upon development expenses incurred by both companies during the term of the agreement will be funded by sanofi-aventis. If the collaboration becomes profitable, we will reimburse sanofi-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.

- **VEGF TRAP — Eye Diseases:** VEGF both stimulates angiogenesis and increases vascular permeability. It has been shown in preclinical studies to be a major pathogenic factor in diabetic retinopathy, diabetic macular edema, and age-related macular degeneration, and is believed to be involved in other medical problems affecting the eyes. In January 2005, we and sanofi-aventis amended our collaboration agreement to exclude rights to develop and commercialize the VEGF Trap for eye diseases through local delivery systems. We now have the exclusive right to develop and commercialize the VEGF Trap for eye diseases through local administration to the eye and plan to initiate a clinical trial of the VEGF Trap delivered through intravitreal injection in mid-2005. While use of the VEGF Trap for eye diseases using systemic delivery remains part of our collaboration with sanofi-aventis, we and sanofi-aventis do not currently intend to pursue further clinical development using systemic delivery of VEGF Trap for eye diseases. Two phase 1 clinical trials of the VEGF Trap delivered systemically for the potential treatment of eye diseases were completed in 2004. We expect to discuss the results from these trials at scientific conferences in 2005.
- **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 may play an important role in a number of rheumatological and other diseases and disorders, including diseases associated with inflammation in blood vessels.

  In October 2003, we announced that the IL-1 Trap demonstrated evidence of clinical activity and safety in patients with rheumatoid arthritis in a phase 2 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. Patients in this trial experienced

statistically significant reductions in c-reactive protein (CRP) levels, and the improvements in CRP levels demonstrated a clear dose response to the IL-1 Trap. The IL-1 Trap was generally well tolerated and no serious drug-related adverse events were reported.

In mid-2005, we plan to further evaluate the safety and efficacy of the IL-1 Trap in rheumatoid arthritis in a double-blind, placebo-controlled, multi-center trial. This trial will be conducted in a larger patient population, testing higher doses of IL-1 Trap for a longer period of time than the phase 2 trial completed in 2003. We expect to evaluate doses of 160 milligrams and 320 milligrams of IL-1 Trap delivered subcutaneously once a week. Additional trials of the IL-1 Trap will be required to support an application seeking approval to market the IL-1 Trap in rheumatoid arthritis.

In the fourth quarter of 2004, we initiated a pilot study of the IL-1 Trap in patients with *CIAS1*-Associated Periodic Syndrome (CAPS), a spectrum of rare diseases associated with mutations in the *CIAS1* gene. IL-1 appears to play a significant role in these diseases. In December 2004, the FDA granted orphan drug status to the IL-1 Trap for the treatment of these diseases. We expect to commence an additional trial for this indication in 2005.

We believe blocking IL-1 could be useful in many potential indications where inflammation plays a role. Examples include such indications as osteoarthritis, certain rare genetic diseases, Still's disease, cardiovascular diseases, and many others. In 2005, we plan to initiate several proof-of-concept studies to identify where the IL-1 Trap demonstrates evidence of efficacy and safety.

- **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. Based on preclinical data, IL-4 and IL-13 are thought to play a major role in diseases such as asthma, allergic disorders, and other inflammatory diseases. At a scientific conference during the second quarter of 2004, we presented the results of a placebo-controlled, double-blind, dose escalation phase 1 trial of the IL-4/13 Trap using subcutaneous injections in adult subjects with mild to moderate asthma. The IL-4/13 Trap was generally safe and well tolerated at the doses tested. We plan to initiate a phase 2 trial in 2005 to evaluate the safety and potential efficacy of the IL-4/13 Trap in asthma or allergy indications.

Our Areas of Focus

Anti-Angiogenesis/Angiogenesis in Cancer, Eye Disease, 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. In addition, repairing leaky vessels can reverse swelling and edema. Reciprocally, blocking tumor-induced angiogenesis can blunt tumor growth.

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 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 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. 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.

VEGF both stimulates angiogenesis and increases vascular permeability, has been shown in preclinical studies 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.

Clinical Development. We discovered and are developing a protein-based product candidate designed to bind to VEGF called the VEGF Trap. As described above, we are currently developing the VEGF Trap in cancer indications in collaboration with sanofi-aventis. We have the exclusive right to develop and commercialize the VEGF Trap for the treatment of eye diseases utilizing local delivery to the eye, such as through intravitreal injections.

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, called 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-18 Trap (designed to block IL-18), and the IL-4/13 Trap (designed to block IL-4 and IL-13).

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, we believe our Cytokine 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 a research program underway for an IL-18 Trap. 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-6, 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. We discovered and are developing a protein-based blocker of IL-1 called the IL-1 Trap in a number of diseases where IL-1 may play an important role, including rheumatoid arthritis, osteoarthritis, *CIAS1*-Associated Periodic Syndrome (CAPS), and certain systemic inflammatory diseases. An IL-1 receptor antagonist, Kineret® (a registered trademark of Amgen Inc.), has been approved by the FDA for the treatment of rheumatoid arthritis. 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.

IL-1 also appears to play an important role in *CIAS1*-Associated Periodic Syndromes (CAPS). These rare genetic disorders, including Familial Cold Auto-Inflammatory Syndrome (FCAS), Muckle Wells Syndrome, and Neonatal Onset Multisystem Inflammatory Disorder (NOMID), affect a small group of people, estimated to be between several hundred to a few thousand. Patients with these disorders develop fever, joint aches, headaches, and rashes. In certain indications, these symptoms can be extremely serious. There are no currently approved therapies for CAPS.

IL-4/13 Trap. We discovered 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. 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 are developing the IL-4/13 Trap in settings of asthma and allergy.

It has been estimated that 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, however, it is thought that excess levels of IL-4 and IL-13 causes over activity of the immune system, which contributes to disease initiation and progression.

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. AXOKINE® is a protein-based product candidate we discovered that is designed to act on the area of the brain region regulating appetite and energy expenditure. We are continuing research and pre-clinical activities in support of AXOKINE, but no new clinical trials are planned at this time.

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 treatment that has beneficial effects on skeletal muscle could have significant clinical benefit. Our muscle research 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. We plan to begin clinical trials of the IL-1 Trap in osteoarthritis during 2005. In addition, 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 in preclinical studies that mutations in this growth factor receptor system cause inherited defects in cartilage development in humans. Thus, we believe 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

In our discovery and development activities, we utilize various 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 possibility 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 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 has agreed to pay us up to $4.0 million annually through December 2007, subject to early termination by Serono with not less than nine months advance notice.

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 led to our discovery of the Angiopoietin 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.

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 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 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 collaboration and licensing agreements with various companies, including sanofi-aventis, Novartis Pharma AG, and Procter & Gamble. 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.

The sanofi-aventis Group. In September 2003, we entered into a collaboration agreement with the sanofi-aventis Group 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. Sanofi-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.

In January 2005, we and sanofi-aventis amended the collaboration agreement to exclude from the scope of the collaboration the development and commercialization of the VEGF Trap for eye diseases through local delivery systems. In connection with the amendment, sanofi-aventis made a one-time payment to us of

$25.0 million in January 2005 of which 50% is repayable to sanofi-aventis following commercialization of the VEGF Trap in accordance with the terms of the amendment.

Under the collaboration agreement, as amended, we and sanofi-aventis will share co-promotion rights and profits on sales, if any, of the VEGF Trap for disease indications included in our collaboration. In December 2004, we earned a $25.0 million payment from sanofi-aventis, which was received in January 2005, upon the 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. Sanofi-aventis has agreed to be responsible for providing commercial scale manufacturing capacity for the VEGF Trap.

Under the collaboration agreement, as amended, agreed upon development expenses incurred by both companies during the term of the agreement will be funded by sanofi-aventis. If the collaboration becomes profitable, we will reimburse sanofi-aventis for 50% of these development expenses, including 50% of the $25.0 million payment received in connection with the January 2005 amendment to our collaboration agreement, 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. Since inception of the collaboration through December 31, 2004, we and sanofi-aventis have incurred $86.5 million in development expenses related to the VEGF Trap program. In addition, if the first commercial sale of a VEGF Trap product for disease of the eye through local delivery systems predates the first commercial sale of a VEGF Trap product under the collaboration by two years, we will begin reimbursing sanofi-aventis for up to $7.5 million of VEGF Trap development expenses in accordance with a formula until the first commercial VEGF Trap sale under the collaboration occurs.

Sanofi-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 sanofi-aventis for 50% of the VEGF Trap development expenses will 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.

Development expenses incurred in 2003 were shared equally by the Company and Novartis. We funded our share of 2003 development expenses through loans from Novartis. In March 2004, Novartis forgave its outstanding loans to us totaling $17.8 million, including accrued interest, based on Regeneron's achieving a pre-defined development milestone, which was recognized as a research progress payment.

In February 2004, Novartis provided notice of its intention not to proceed with the joint development of the IL-1 Trap. In March 2004, Novartis agreed to pay the Company $42.75 million to satisfy its obligation to fund development costs for the IL-1 Trap for the nine month period following its notification and for the two months prior to that notice. We recorded the $42.75 million as other contract income in the first quarter of 2004. In addition, we recognized contract research and development revenue of $22.1 million, which represents the remaining amount of the March 2003 up-front payment from Novartis that had previously been deferred. Regeneron and Novartis each retain rights under the collaboration agreement to elect to collaborate in the future on the development and commercialization of certain other IL-1 antagonists.

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 purchases of our Common Stock of $42.9 million in June 1997 and $17.1 million in August 2000. These 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 $90.8 million through December 31, 2004. 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 2001, research support from Procter & Gamble is $2.5 million per quarter (plus annual 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.

Manufacturing

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, as amended, expires in 2006. 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. At December 31, 2004, we employed 287 people at these owned and leased manufacturing facilities. As of December 31, 2004, there were no impairment losses associated with long-lived assets.

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. In February 2005, we and Merck extended the Merck Agreement through October 2006 and provided Merck an opportunity, upon twelve-months' prior notice, to extend the Merck Agreement for an additional year through October 2007. Under the Merck Agreement, as amended, we are manufacturing intermediate for Merck for seven years, with certain minimum order quantities each year. The Merck Agreement may be terminated at any time by Merck upon Merck's payment of a termination fee. 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 (plus annual adjustments 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 $18.1 million in 2004, $10.1 million in 2003, and $11.1 million in 2002.

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., Eyetech Pharmaceuticals, Inc., Abbott Laboratories, sanofi-aventis, 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 antibodies to VEGF, antibodies to the VEGF receptor, small molecule antagonists to the VEGF receptor tyrosine kinase, and 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, in February 2004, Genentech was granted approval by the FDA to market and sell Avastin™, a monoclonal antibody to VEGF in patients with colorectal cancer. The marketing approval for Avastin may make it more difficult for us to enroll patients in clinical trials to support the VEGF Trap oncology program. This may delay or impair our ability to successfully develop and commercialize the VEGF Trap. Novartis has an ongoing phase 3 clinical development program evaluating a VEGF tyrosine kinase in different cancer settings.

The VEGF Trap also faces significant competition in the treatment of eye diseases. For example, Eyetech Pharmaceuticals is collaborating with Pfizer to further develop and commercialize a VEGF inhibitor for eye diseases, which was recently approved by the FDA. Genentech and Novartis have a phase 3 program nearing completion that is evaluating a VEGF blocker in patients with eye diseases. Successful development of these competing VEGF blockers would also make it more difficult for us to enroll patients in clinical trials for the VEGF Trap in these indications and may delay or impair our ability to successfully develop and commercialize the VEGF Trap.

IL-1 Trap/ IL-4/13 Trap. 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 drugs 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), and the IL-1 receptor antagonist Kineret® (a registered trademark of Amgen), 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.

Other Areas. Many pharmaceutical and biotechnology companies are attempting to discover new therapeutics for indications in which we invest substantial time and resources. Some are trying to 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, obesity, 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.

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 an adverse effect on our operations, or future prospects, or the market 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 or other consideration for use of their technology. These institutions are becoming more active in seeking patent protection and licensing arrangements to collect royalties or other consideration 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 our business and operations. 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 Cytokine Traps, VEGF Trap, AXOKINE, 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 in August 2004, we made a cash payment to Merck of $0.6 million. 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 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.

Approval of a product candidate by comparable regulatory authorities in foreign countries is generally required prior to commencement of marketing of the product in those countries. The approval procedure varies among countries and may involve additional testing, and the time required to obtain such approval may differ from that required for FDA approval.

Various federal, state, and foreign 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, 2004, we had 730 full-time employees, of whom 115 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 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 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 and office 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	$ 188,000	none
Tarrytown	16,000	December 31, 2007	$ 25,000	none
Tarrytown	74,000	December 31, 2009	$ 145,000	one 5-year term
Rensselaer	75,000	July 11, 2007	$ 25,000	two 5-year terms

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

We believe that our existing owned and leased facilities are adequate for ongoing, research, development, manufacturing, and administrative activities.

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, purported class action securities 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. On February 1, 2005, the United States District Court for the Southern District of New York denied our motion to dismiss the consolidated amended complaint. We believe that the lawsuit is without merit and intend to continue to defend the action vigorously. Because we do not believe that a loss is probable, no legal reserve has been established. However, we cannot assure investors that we will be successful in defending this action, or that the amount of any settlement or judgment in this action will not exceed the coverage limits of our director and officer liability insurance policies. If we are not successful in defending this action, our business and financial condition could be adversely affected. In addition, whether or not we are successful, the defense of this action may divert the attention of our management and other resources that would otherwise be engaged in running our business.

From time to time we are a party to other legal proceedings in the course of our business. 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***

On December 17, 2004, we conducted a Special Meeting of Shareholders pursuant to due notice. A quorum being present either in person or by proxy, the shareholders voted on the following matters:

1. To amend Regeneron's 2000 Long-Term Incentive Plan to expressly authorize the Option Exchange Program described in the proxy statement dated November 29, 2004.

No other matters were voted on. The number of votes cast was:

	For	Against	Abstain
Approval of Amendment to the 2000 Long-Term Incentive Plan to Authorize the Option Exchange Program	46,029,856	16,697,527	53,532

PART II

Item 5. *Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities*

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
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
2004		
First Quarter	$ 17.00	$ 12.80
Second Quarter	15.85	8.53
Third Quarter	10.80	6.76
Fourth Quarter	9.49	6.75

As of February 28, 2005, there were 616 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 $6.11.

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

The information under the heading "Equity Compensation Plan Information" in our definitive proxy statement with respect to our 2005 Annual Meeting of Shareholders to be filed with the SEC is incorporated by reference into Item 12 of this Report on Form 10-K.

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

The selected financial data set forth below for the years ended December 31, 2004, 2003, and 2002 and at December 31, 2004 and 2003 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, 2001 and 2000 and at December 31, 2002, 2001, and 2000 are derived from our audited financial statements not included in this report.

	Year Ended December 31,				
	2004	2003	2002	2001	2000
	(In thousands, except per share data)				
Statement of Operations Data					
Revenues					
Contract research and development	$ 113,157	$ 47,366	$ 10,924	$ 12,071	$ 36,478
Research progress payments	42,770				6,200
Contract manufacturing	18,090	10,131	11,064	9,902	16,598
	174,017	57,497	21,988	21,973	59,276
Expenses					
Research and development(1)	136,095	136,024	124,953	92,542	65,134
Contract manufacturing	15,214	6,676	6,483	6,509	15,566
General and administrative	17,062	14,785	12,532	9,607	8,427
	168,371	157,485	143,968	108,658	89,127
Income (loss) from operations	5,646	(99,988)	(121,980)	(86,685)	(29,851)
Other income (expense)					
Other contract income	42,750				
Investment income	5,478	4,462	9,462	13,162	8,480
Interest expense	(12,175)	(11,932)	(11,859)	(2,657)	(281)
	36,053	(7,470)	(2,397)	10,505	8,199
Net income (loss) before cumulative effect of a change in accounting principle	41,699	(107,458)	(124,377)	(76,180)	(21,652)
Cumulative effect of adopting Staff Accounting Bulletin 101 ("SAB 101")(2)					(1,563)
Net income (loss)	$ 41,699	$ (107,458)	$ (124,377)	$ (76,180)	$ (23,215)
Net income (loss) per share, basic:					
Before cumulative effect of a change in accounting principle	$ 0.75	$ (2.13)	$ (2.83)	$ (1.81)	$ (0.62)
Cumulative effect of adopting SAB 101					(0.04)
Net income (loss) per share	$ 0.75	$ (2.13)	$ (2.83)	$ (1.81)	$ (0.66)
Net income (loss) per share, diluted	$ 0.74	$ (2.13)	$ (2.83)	$ (1.81)	$ (0.66)

(1) Includes Income (Loss) in Amgen-Regeneron Partners of $134, ($63), ($27), ($1,002), and ($4,575) for the years ended December 31, 2004, 2003, 2002, 2001, and 2000, respectively.

(2) See Note 2 to our audited financial statements.

	At December 31,				
	2004	2003	2002	2001	2000
			(In thousands)		
Balance Sheet Data					
Cash, cash equivalents, marketable securities, and restricted marketable securities (current and non-current)	$ 348,912	$ 366,566	$ 295,246	$ 438,383	$ 154,370
Total assets	473,108	479,555	391,574	495,397	208,274
Capital lease obligations and notes payable, long-term portion	200,000	200,000	200,000	200,150	2,069
Stockholders' equity	182,543	137,643	145,981	266,355	182,130

Item 7. ***Management's Discussion and Analysis of Financial Condition and Results of Operations***

Overview

We are a biopharmaceutical company that discovers, develops, and intends to commercialize pharmaceutical products for the treatment of serious medical conditions. We are currently conducting clinical programs for the VEGF Trap, IL-1 Trap, and IL-4/13 Trap, which are in various stages of development. In addition to our clinical programs, we have research programs focused on angiogenesis, metabolic diseases, muscle atrophy and related disorders, inflammatory conditions, and other diseases and disorders. We also use our Velocigene® and Trap technology platforms to discover and develop new product candidates and are developing our Velocimmune™ platform to create fully human, therapeutic antibodies.

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 and may never receive such revenues. Before revenues from the commercialization of our product candidates can be realized, we (or our collaborators) must overcome a number of hurdles which include successfully completing research and development and obtaining regulatory approval from the FDA and regulatory authorities in other countries. In addition, the biotechnology and pharmaceutical industries are rapidly evolving and highly competitive, and new developments may render our products and technologies uncompetitive or obsolete.

From inception on January 8, 1988 through December 31, 2004, we had a cumulative loss of $489.8 million. In the absence of revenues from the commercialization of our product candidates or other sources, the amount, timing, nature, or source of which cannot be predicted, our losses will continue as we conduct our research and development activities. We expect to incur substantial losses over the next several years as we continue the clinical development of the VEGF Trap, IL-1 Trap, and IL-4/13 Trap; advance new product candidates into clinical development from our existing research programs; continue our research and development programs; and commercialize product candidates that receive regulatory approval, if any.

Our activities may expand over time and may require additional resources, and we expect our operating losses to 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 progress of our research and development efforts, the timing of certain expenses, and the amount and timing of payments that we receive from collaborators.

As a company that does not expect to generate product revenues or profits over the next several years, management of cash flow is extremely important. The most significant use of our cash is for research and development activities, which include drug discovery, preclinical studies, clinical trials, and the manufacture of drug supplies for preclinical studies and clinical trials. In 2004, our research and development expenses totaled $136.1 million. We expect these expenses, exclusive of non-cash expenses related to grants of stock options, to increase 40-60% in 2005, depending on the progress of our clinical programs. The principal sources of cash to-date have been sales of common equity and convertible debt and funding from our collaborators in the form of up-front payments, research progress payments, payments for our research and development activities, and purchases of our common stock. We also receive payments for contract manufacturing.

A primary driver of our expenses is our number of full-time employees. Our annual average headcount in 2004 was 721 compared to 675 in 2003 and 643 in 2002. In 2005, we expect our average headcount to increase to approximately 775, primarily to support our research and development programs.

The planning, execution, and results of our clinical programs are significant factors that can affect our operating and financial results. In our clinical programs, key events in 2004 and plans for 2005 are as follows:

Product Candidate	2004 Events	2005 Plans
VEGF Trap — Oncology	• Completed phase 1 subcutaneous single-agent trial in cancer • Commenced phase 1 intravenous single-agent trial in cancer • Received Fast Track designation for VEGF Trap for specific niche cancer indication	• Commence additional single-agent and combination trials in cancer
VEGF Trap — Eye Diseases	• Completed treatment portion of phase 1 intravenous single-agent trial in neovascular age-related macular degeneration • Completed treatment portion of phase 1 intravenous single-agent trial in diabetic macular edema	• Commence studies in eye diseases utilizing local delivery systems, such as intraocular injections
IL-1 Trap	• Planned for future trials in rheumatoid arthritis • Completed treatment phase of single-dose patient tolerability studies to evaluate new formulations • Commenced proof-of-concept study in *CIAS1*-Associated Periodic Syndrome (CAPS) • Received FDA Orphan designation for the IL-1 Trap in treatment of CAPS	• Commence clinical trial in rheumatoid arthritis • Commence clinical trial in osteoarthritis • Commence exploratory proof of concept trials in other indications • Complete CAPS proof-of-concept study and commence additional trial in this indication • Evaluate IL-1 Trap in other inflammatory conditions
IL-4/13 Trap	• Completed phase 1 trial in asthma	• Commence clinical trial in asthma or allergy indication

In September 2003, we entered into a collaboration agreement with the sanofi-aventis Group to collaborate on the development and commercialization of the VEGF Trap. Sanofi-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.

In January 2005, we and sanofi-aventis amended our collaboration agreement to exclude rights to develop and commercialize the VEGF Trap for eye diseases through local delivery systems. In connection with this amendment, sanofi-aventis made a $25.0 million non-refundable payment to us.

Under the collaboration agreement, as amended, we and sanofi-aventis will share co-promotion rights and profits on sales, if any, of the VEGF Trap for disease indications included in our collaboration. In December 2004, we earned a $25.0 million payment from sanofi-aventis, which was received in January 2005, upon the 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. Sanofi-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 sanofi-aventis. If the collaboration becomes profitable, we will reimburse sanofi-aventis for 50% of the VEGF Trap development expenses, including 50% of the $25.0 million payment received in connection with the January 2005 amendment to our collaboration agreement, 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. Since inception of the collaboration through December 31, 2004, we and sanofi-aventis have incurred $86.5 million in development expenses related to VEGF Trap program. In addition, if the first commercial sale of a VEGF Trap product for disease of the eye through local delivery systems predates the first commercial sale of a VEGF Trap product under the collaboration by two years, we will begin reimbursing sanofi-aventis for up to $7.5 million of VEGF Trap development expenses in accordance with a formula until the first commercial VEGF Trap sale under the collaboration occurs.

Sanofi-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 sanofi-aventis for 50% of the VEGF Trap development expenses will terminate and we will retain all rights to the VEGF Trap.

In March 2003, we entered into a collaboration agreement with Novartis Pharma AG to jointly develop and commercialize the IL-1 Trap. Novartis made a non-refundable payment of $27.0 million and purchased 7,527,050 newly issued unregistered shares of our Common Stock for $48.0 million. In February 2004, Novartis provided notice of its intention not to proceed with the joint development of the IL-1 Trap, and subsequently paid us $42.75 million to satisfy its obligation to fund development costs for the nine month period following its notification and for the two months prior to that notice. All rights to the IL-1 Trap have reverted to Regeneron. Novartis and we retain rights under the collaboration agreement to elect to collaborate in the future on the development and commercialization of certain other IL-1 antagonists. In March 2004, we also achieved a pre-defined development milestone and Novartis forgave all its outstanding development expense loans to us, totaling $17.8 million.

Results of Operations

Years Ended December 31, 2004 and 2003

Revenues:

Revenues for the years ended December 31, 2004 and 2003 consist of the following:

	2004	2003
	(In millions)	
Contract research & development revenue		
Sanofi-aventis	$ 78.3	$ 14.3
Novartis	22.1	21.4
Procter & Gamble	10.5	10.6
Other	2.2	1.1
Total contract research & development revenue	113.1	47.4
Research progress payments		
Sanofi-aventis	25.0	—
Novartis	17.8	—
Total research progress payments	42.8	—
Contract manufacturing revenue	18.1	10.1
Total revenue	$ 174.0	$ 57.5

Our total revenue increased to $174.0 million in 2004 from $57.5 million in 2003 primarily due to higher revenues related to our collaboration with sanofi-aventis on the VEGF Trap and our prior collaboration with Novartis on the IL-1 Trap. Collaboration revenue earned from sanofi-aventis and Novartis is comprised of contract research and development revenue and research progress payments. Contract research and development revenue, as detailed below, consists partly of reimbursement for research and development expenses and partly of the recognition of revenue related to non-refundable, up-front payments. Non-refundable up-front payments are recorded as deferred revenue and recognized ratably over the period over which we are obligated to perform services in accordance with SAB 104 (see Critical Accounting Policies and Significant Judgments and Estimates). In the first quarter of 2004, Novartis provided notice of its intention not to proceed with the joint development of the IL-1 Trap and the $22.1 million remaining balance of the $27.0 million up-front payment received from Novartis in March 2003 was recognized as contract research and development revenue.

Sanofi-aventis and Novartis contract research & development revenues for 2004 and 2003 were as follows:

	2004 Regeneron Expense Reimbursement	Up-front Payment to Regeneron			Total Revenue Recognized in 2004
		Total Payment	Amount Recognized in 2004	Deferred Revenue at December 31, 2004	
			(In millions)		
Sanofi-aventis	$ 67.8	$ 80.0	$ 10.5	$ 65.8	$ 78.3
Novartis	—	27.0	22.1	—	22.1
Total	$ 67.8	$ 107.0	$ 32.6	$ 65.8	$ 100.4

	2003 Regeneron Expense Reimbursement	Up-front Payment to Regeneron			Total Revenue Recognized in 2004
		Total Payment	Amount Recognized in 2004	Deferred Revenue at December 31, 2004	
			(In millions)		
Sanofi-aventis	$ 10.7	$ 80.0	$ 3.6	$ 76.4	$ 14.3
Novartis	16.5	27.0	4.9	22.1	21.4
Total	$ 27.2	$ 107.0	$ 8.5	$ 98.5	$ 35.7

In December 2004, we earned a $25.0 million research progress payment from sanofi-aventis, which was received in January 2005, upon achievement of an early-stage VEGF Trap clinical milestone. In March 2004, Novartis forgave all its outstanding loans, including accrued interest, to Regeneron totaling $17.8 million, based upon Regeneron's achieving a pre-defined IL-1 Trap development milestone. These amounts were recognized as research progress payments in 2004.

Contract manufacturing revenue relates to our long-term agreement with Merck to manufacture a vaccine intermediate at our Rensselaer, New York facility. Contract manufacturing revenue increased to $18.1 million in 2004 from $10.1 million in 2003, principally due to an increase in product shipments to Merck in 2004 compared to 2003. Revenue and the related manufacturing expense are recognized as product is shipped, after acceptance by Merck. Included in contract manufacturing revenue in 2004 and 2003 are $3.6 million and $1.7 million, respectively, of deferred revenue associated with capital improvement reimbursements paid by Merck prior to commencement of production. This deferred revenue is being recognized as product is shipped to Merck based on the total amount of product expected to be shipped over the life of the manufacturing agreement. In February 2005, we agreed to extend the manufacturing agreement by one year through October 2006 and provide Merck an opportunity, upon twelve months' prior notice, to extend the agreement for an additional year through October 2007.

Research and Development Expenses:

Research and development expenses increased slightly to $136.1 million in 2004 from $136.0 million in 2003. The following table summarizes the major categories of our research and development expenses for the years ended December 31, 2004 and 2003:

	2004	2003
	(In millions)	
Research and development expenses:		
Payroll and benefits	$ 43.6	$ 38.5
Clinical trial expenses	10.3	25.0
Clinical manufacturing costs(1)	36.4	29.8
Research and preclinical development costs	23.1	19.6
Occupancy and other operating costs	22.7	23.1
Total research and development	$ 136.1	$ 136.0

(1) Represents the full cost of manufacturing drug for use in research, preclinical development and clinical trials, including related payroll and benefits, manufacturing materials and supplies, depreciation, and occupancy costs of our Rensselaer manufacturing facility.

Payroll and benefits increased $5.1 million in 2004 compared with 2003 as we added research and development personnel to support our clinical and research programs, especially for the VEGF Trap and IL-1 Trap. Clinical trial expenses decreased $14.7 million in 2004 from 2003 due primarily to the completion of the double-blind treatment portion of our AXOKINE phase 3 clinical trial for the treatment of obesity in 2003, the completion of other AXOKINE trials in 2004, and the completion of our IL-4/13 Trap phase 1 trial in 2004. These decreases were partly offset by higher clinical trial expenses related to our VEGF Trap and IL-1 Trap clinical programs. Clinical manufacturing costs increased $6.6 million in 2004 compared to 2003 as we manufactured supplies of our clinical product candidates in our expanded Rensselaer manufacturing facility for the full year of 2004. Research and preclinical development costs increased $3.5 million due primarily to higher preclinical development costs related to our VEGF Trap program and higher research-related costs for outside services in 2004 than in 2003. Occupancy and other operating costs decreased slightly by $0.4 million in 2004 compared to 2003 primarily as a result of lower depreciation costs due to extending the lease on our Tarrytown, New York facilities in early 2004.

Contract Manufacturing Expenses:

Contract manufacturing expenses increased to $15.2 million in 2004, compared to $6.7 million in 2003, primarily because more product was shipped to Merck in 2004 and the Company incurred unfavorable manufacturing costs, which were expensed in the period incurred, in 2004 compared to 2003.

General and Administrative Expenses:

General and administrative expenses increased to $17.1 million in 2004 from $14.8 million in 2003, due primarily to a $1.4 million increase in professional fees, principally associated with accounting and other services related to our efforts to comply with the requirements of Section 404 of the Sarbanes-Oxley Act of 2002. The remainder of the 2004 increase was principally due to increases in payroll and related costs associated, in part, with higher administrative headcount in 2004 to support the Company's operations.

Other Income and Expense:

In the first quarter of 2004, Novartis notified us of its decision to forego its right under our collaboration to jointly develop the IL-1 Trap and agreed to pay us $42.75 million to satisfy its obligation to fund development costs for the IL-1 Trap for the nine-month period following its notification and for the two

months prior to that notice. The $42.75 million was included in other contract income in the first quarter of 2004.

Investment income increased to $5.5 million in 2004 from $4.5 million in 2003 due primarily to higher effective interest rates on investment securities. Interest expense increased slightly to $12.2 million in 2004 from $11.9 million in 2003. Interest expense is attributable primarily to $200.0 million of convertible notes issued in October 2001, which mature in 2008 and bear interest at 5.5% per annum.

Years Ended December 31, 2003 and 2002

Revenues:

Revenues for the years ended December 31, 2003 and 2002 consist of the following:

	2003	2002
	(In millions)	
Contract research & development revenue		
Novartis	$ 21.4	$ —
Sanofi-aventis	14.3	—
Procter & Gamble	10.6	10.5
Other	1.1	0.4
Total contract research & development revenue	47.4	10.9
Contract manufacturing revenue	10.1	11.1
Total revenue	$ 57.5	$ 22.0

Our total revenue increased to $57.5 million in 2003 from $22.0 million in 2002 primarily from the recognition of $21.4 million of revenue related to our collaboration with Novartis on the IL-1 Trap and $14.3 million of revenue related to our collaboration with sanofi-aventis on the VEGF Trap. This collaboration revenue, as detailed below, consists partly of reimbursement for research and development expenses and partly of the recognition of revenue related to non-refundable up-front payments. Non-refundable up-front payments are recorded as deferred revenue and recognized ratably over the period over which we are obligated to perform services in accordance with SAB 104 (see Critical Accounting Policies and Significant Judgments and Estimates).

Sanofi-aventis and Novartis contract research & development revenues for 2003 were as follows:

	2003 Regeneron Expense Reimbursement	Up-front Payment to Regeneron			Total Revenue Recognized in 2003
		Total Payment	Amount Recognized in 2003	Deferred Revenue at December 31, 2003	
			(In millions)		
Novartis	$ 16.5	$ 27.0	$ 4.9	$ 22.1	$ 21.4
Sanofi-aventis	10.7	80.0	3.6	76.4	14.3
Total	$ 27.2	$ 107.0	$ 8.5	$ 98.5	$ 35.7

Contract manufacturing revenue relates to our long-term agreement with Merck. Contract manufacturing revenue decreased to $10.1 million in 2003 from $11.1 million in 2002, due primarily to the receipt of a non-recurring $1.0 million payment in the third quarter of 2002 related to services we provided to Merck in prior years. Revenue and the related manufacturing expense are recognized as product is shipped, after acceptance by Merck. Included in contract manufacturing revenue in 2003 and 2002 are $1.7 million and $1.8 million, respectively, of deferred revenue associated with capital improvement reimbursements paid by Merck prior to commencement of production. This deferred revenue is being recognized as product is shipped to Merck based on the total amount of product expected to be shipped over the life of the agreement.

Research and Development Expenses:

Research and development expenses increased to $136.0 million in 2003 from $125.0 million in 2002. The following table summarizes the major categories of our research and development expenses for the years ended December 31, 2003 and 2002:

	2003	2002
	(In millions)	
Research and development expenses:		
Payroll and benefits	$ 38.5	$ 35.9
Clinical trial expenses	25.0	33.9
Clinical manufacturing costs(1)	29.8	17.3
Research and preclinical development costs	19.6	18.4
Occupancy and other operating costs	23.1	19.5
Total research and development	$ 136.0	$ 125.0

(1) Represents the full cost of manufacturing drug for use in research, preclinical development and clinical trials, including related payroll and benefits, manufacturing materials and supplies, depreciation, and occupancy costs of our Rensselaer manufacturing facility.

Payroll and benefits increased $2.6 million in 2003 compared with 2002 as we added research and regulatory personnel to support our clinical and research programs. Clinical trial expenses decreased $8.9 million in 2003 from 2002 due primarily to the completion of the double-blind treatment portion of the AXOKINE phase 3 trial in January of 2003. Clinical manufacturing costs increased $12.5 million in 2003 compared to 2002. In 2003 we completed an expansion to our Rensselaer, New York plant, and leased additional warehouse and manufacturing facilities nearby, to increase our capacity to manufacture supplies of our product candidates. As a result, we added manufacturing personnel, purchased more materials and supplies, and incurred higher depreciation and occupancy costs for our manufacturing facilities in 2003 compared to 2002. Research and preclinical development costs increased $1.2 million in 2003 compared to 2002 due primarily to expense recognized in connection with a license agreement granted to us by Merck in 2003 related to the development of AXOKINE. Occupancy and other operating costs increased $3.6 million in 2003 compared to 2002 due primarily to higher costs for the full year 2003 related to leasing additional lab and office space in Tarrytown in the third quarter of 2002, and higher depreciation costs associated with leasehold renovations completed in 2003.

Contract Manufacturing Expenses:

Contract manufacturing expenses increased to $6.7 million in 2003, compared to $6.5 million in 2002, primarily because we shipped more product to Merck.

General and Administrative Expenses:

General and administrative expenses increased to $14.8 million in 2003 from $12.5 million in 2002, due primarily to (i) a $1.0 million increase in payroll related costs, (ii) a $0.8 million increase in professional fees, principally associated with legal expenses for general corporate matters and the collaborations with sanofi-aventis and Novartis, and (iii) a $0.5 million increase in operating expenses including rent, utilities, supplies, and insurance.

Other Income and Expense:

Investment income decreased to $4.5 million in 2003 from $9.5 million in 2002 due primarily to lower effective interest rates on investment securities. In addition, our levels of interest-bearing investments were lower for most of 2003 as we funded our operations. Interest expense was $11.9 million in both 2003 and 2002.

Interest expense is attributable primarily to $200.0 million of convertible notes issued in October 2001, which mature in 2008 and bear interest at 5.5% per annum.

Liquidity and Capital Resources

Since our inception in 1988, we have financed our operations primarily through offerings of our equity securities, a private placement of convertible debt, revenue earned under our past and present research and development and contract manufacturing agreements, including our agreements with Aventis, Novartis, Procter & Gamble, and Merck, and investment income.

Years Ended December 31, 2004 and 2003

Cash Used in Operations:

At December 31, 2004, we had $348.9 million in cash, cash equivalents, and marketable securities compared with $366.6 million, which included $10.9 million of restricted marketable securities, at December 31, 2003. In January 2005, we received two $25.0 million payments from sanofi-aventis. One payment was related to a VEGF Trap clinical milestone that was earned in 2004. The second payment related to changes to our collaboration agreement with sanofi-aventis that were made in January 2005. Restricted marketable securities consisted of pledged U.S. government securities which were sufficient upon receipt of scheduled principal and interest payments to provide for the payment in full of the interest payments on the convertible senior subordinated notes through October 2004.

Net cash used in operations was $16.9 million in 2004 compared to $6.1 million in 2003. The increase in cash used in operations during 2004 was primarily due to the 2003 receipt of non-refundable up-front payments associated with the sanofi-aventis and Novartis collaborations, offset in part by higher 2004 receipts from (i) sanofi-aventis for contract research and development revenue and (ii) Novartis for its $42.75 million payment to us following its first quarter 2004 decision to forego its right under our collaboration to jointly develop the IL-1 Trap. The majority of cash used in operations in both 2004 and 2003 was to fund research and development, primarily related to our VEGF Trap and IL-1 Trap programs.

In September 2003, we entered into a collaboration agreement with sanofi-aventis to jointly develop and commercialize the VEGF Trap. Sanofi-aventis made a non-refundable up-front payment of $80.0 million which was recorded to deferred revenue and is being recognized as contract research and development revenue ratably over the period during which we expect to perform services. In 2004 and 2003, we recognized $10.5 million and $3.6 million of revenue, respectively, related to this up-front payment and we anticipate, based on current VEGF Trap product development plans, that we will recognize approximately $9.4 million of revenue over each of the next 7 years. Sanofi-aventis has agreed to fund all agreed upon development expenses incurred by both companies in connection with indications included in our collaboration during the term of the agreement. Sanofi-aventis funded $67.8 million of our VEGF Trap development costs in 2004 and $10.7 million in 2003, of which $13.9 million and $8.9 million, respectively, were included in accounts receivable as of December 31, 2004 and 2003. In addition, in December 2004 we earned a $25.0 million milestone payment from sanofi-aventis, which was also included in accounts receivable at December 31, 2004.

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 which was initially recorded to deferred revenue. In 2003, we recognized $4.9 million of revenue related to this up-front payment. In the first quarter of 2004, Novartis provided notice of its intention not to proceed with the joint development of the IL-1 Trap and the remaining balance of the $27.0 million up-front payment, or $22.1 million, was recognized as contract research and development revenue. As described above, we also received a $42.75 million payment from Novartis in the first quarter of 2004 which was recognized as other contract income. In addition, in March 2004, Novartis forgave all its outstanding loans, including accrued interest, to Regeneron totaling $17.8 million, based upon Regeneron's achieving a pre-defined IL-1 Trap development milestone. Development expenses incurred during 2003 were shared equally by Regeneron and Novartis. In 2003, Novartis agreed to reimburse us for $16.5 million of our IL-Trap development costs, of which $3.2 million was included in accounts receivable as of December 31, 2003.

In 2003, we recorded a non-cash expense of $1.5 million associated with the issuance of our Common Stock in connection with a license agreement entered into with Merck.

In both 2004 and 2003, we made two semi-annual interest payments totaling $11.0 million per year on our convertible senior subordinated notes.

Cash Used in Investing Activities:

Net cash used in investing activities decreased to $4.6 million in 2004 from $63.8 million in 2003, due primarily to a decrease in purchases of marketable securities, net of sales or maturities. In 2004, purchases of marketable securities exceeded sales or maturities by $9.5 million, whereas in 2003, purchases of marketable securities exceeded sales or maturities by $45.2 million. In addition, payments for capital expenditures decreased $23.5 million in 2004 compared to 2003, due primarily to the completion of our Rensselaer plant expansion in 2003.

Cash Provided by Financing Activities:

Cash provided by financing activities decreased to $4.4 million in 2004 from $108.2 million in 2003, due primarily to the sale of Common Stock to sanofi-aventis and Novartis in 2003 in association with the collaboration agreements. Sanofi-aventis purchased 2,799,552 newly issued unregistered shares of our Common Stock for $45.0 million. Novartis purchased 7,527,050 newly issued unregistered shares of our Common Stock for $48.0 million. In addition, in accordance with our collaboration agreement with Novartis, we elected to fund our share of 2003 IL-1 Trap development expenses through a loan from Novartis that was forgiven in March 2004 upon Regeneron's achieving a pre-defined IL-1 Trap development milestone. As of December 31, 2003, we had drawn $13.7 million, excluding interest, against this loan facility and we drew an additional $3.8 million during the first quarter of 2004 for expenses incurred during 2003.

Sanofi-aventis Agreement:

In January 2005, we and sanofi-aventis amended our collaboration agreement to exclude rights to develop and commercialize the VEGF Trap for eye diseases through local delivery systems. In connection with this amendment, sanofi-aventis made a $25.0 million non-refundable payment to us.

Under the collaboration agreement, as amended, we and sanofi-aventis will share co-promotion rights and profits on sales, if any, of the VEGF Trap for disease indications included in our collaboration. In December 2004, we earned a $25.0 million payment from sanofi-aventis, which was received in January 2005, 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.

We have agreed to continue to manufacture clinical supplies of the VEGF Trap at our plant in Rensselaer, New York. Sanofi-aventis has agreed to be responsible for providing commercial scale manufacturing capacity for the VEGF Trap. Under the collaboration agreement, as amended, agreed upon development expenses incurred by both companies during the term of the agreement, including costs associated with the manufacture of clinical drug supply, will be funded by sanofi-aventis. If the collaboration becomes profitable, we will reimburse sanofi-aventis for 50% of these development expenses, including 50% of the $25.0 million payment received in connection with the January 2005 amendment to our collaboration agreement, 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 addition, if the first commercial sale of a VEGF Trap product for diseases of the eye through local delivery systems predates the first commercial sale of a VEGF Trap product under the collaboration, we will begin reimbursing sanofi-aventis for up to $7.5 million of VEGF Trap development expenses commencing two years after such initial commercialization outside the collaboration in accordance with a formula until the first commercial VEGF Trap sale under the collaboration occurs. Since inception of the collaboration agreement through December 31, 2004, we incurred and were subsequently reimbursed by sanofi-aventis for $78.1 million in development expenses related to the VEGF Trap

program. In addition to expenses incurred by us, sanofi-aventis has incurred $8.4 million in development expenses through December 31, 2004 related to the VEGF Trap program.

We and sanofi-aventis plan to initiate multiple clinical studies in 2005 to evaluate the VEGF Trap as both a single-agent and in combination with other therapies in various cancer indications. During the third quarter of 2004, the FDA granted Fast Track designation to the VEGF Trap for a specific niche cancer indication. As a result of the FDA's decision, we and sanofi-aventis plan to initiate a clinical trial in that indication in 2005.

Merck License Agreement:

In August 2003, Merck granted to us a non-exclusive license to certain patents and patent applications which may be used in the development and commercialization of AXOKINE. As consideration, we issued to Merck 109,450 newly issued unregistered shares of our Common Stock (the Merck Shares), valued at $1.5 million based on the fair market value of shares of our Common Stock on the agreement's effective date. In August 2004, we repurchased from Merck, and subsequently retired, the Merck Shares for $0.9 million, based on the fair market value of the shares on August 19, 2004. We also made a cash payment of $0.6 million to Merck as required under the license agreement. The agreement requires us to make an additional payment to Merck upon receipt of marketing approval for a product covered by the licensed patents. In addition, we would be required to pay royalties, at staggered rates in the mid-single digits, based on the net sales of products covered by the licensed patents.

Convertible Debt:

In 2001, we issued $200.0 million aggregate principal amount of convertible senior subordinated notes in a private placement and received proceeds, after deducting the initial purchasers' discount and out-of pocket expenses, of $192.7 million. The notes bear interest at 5.5% per annum, payable semi-annually and mature in 2008. The notes are convertible into shares of our Common Stock at a conversion price of approximately $30.25 per share, subject to adjustment in certain circumstances. We may redeem some or all of the notes if the closing price of our Common Stock has exceeded 140% of the conversion price then in effect for a specified period of time.

As part of this transaction, we pledged $31.6 million of U.S. government securities which was sufficient upon receipt of scheduled principal and interest payments to provide for the payment in full of the first six scheduled interest payments on the notes when due, the last of which was paid in October 2004.

Capital Expenditures:

Our additions to property, plant, and equipment totaled $6.0 million in 2004, $16.9 million in 2003, and $45.9 million in 2002, including a total of $48.0 million in 2002 and 2003 related to the expansion of our manufacturing facilities in Rensselaer, New York, which was completed in 2003. In 2005, we expect to incur approximately $10 million in capital expenditures which primarily consists of equipment for our expanded manufacturing, research, and development activities.

Funding Requirements:

Our total expenses for research and development from inception through December 31, 2004 have been approximately $857 million. We have entered into various agreements related to our activities to develop and commercialize product candidates and utilize our technology platforms, including collaboration agreements, such as with sanofi-aventis, Novartis, and Procter & Gamble, and agreements to use our Velocigene™ technology platform, such as with Serono S.A. We incurred expenses associated with these agreements, which include an allocable portion of general and administrative costs, of $75.3 million, $56.0 million and $11.9 million in 2004, 2003, and 2002, respectively.

We expect to continue to incur substantial funding requirements primarily for research and development activities (including preclinical and clinical testing). We currently anticipate that approximately 55%-65% of our expenditures for 2005 will be directed toward the preclinical and clinical development of product

candidates, including the VEGF Trap, IL-1 Trap, and IL-4/13 Trap; approximately 20%-30% of our expenditures for 2005 will be applied to our basic research activities and the continued development of our novel technology platforms; and the remainder of our expenditures for 2005 will be used for capital expenditures and general corporate purposes.

In connection with our funding requirements, the following table summarizes our contractual obligations as of December 31, 2004 for leases and long-term debt. None of these obligations extend beyond 5 years.

		Payments Due by Period		
	Total	Less than one year	1 to 3 years	4 to 5 years
		(In millions)		
Convertible Senior Subordinated Notes Payable(1)	$ 244.0	$ 11.0	$ 22.0	$ 211.0
Operating Leases(2)	17.7	4.9	9.2	3.6

(1) Includes amounts representing interest.

(2) Excludes future contingent rental costs for utilities, real estate taxes, and operating expenses. In 2004, these costs were $6.0 million.

The amount we need to fund operations will depend on various factors, including the status of competitive products, the success of our research and development programs, the potential future need to expand our professional and support staff and facilities, the status of patents and other intellectual property rights, the delay or failure of a clinical trial of any of our potential drug candidates, and the continuation, extent, and success of any collaborative research and development collaborations (including those with sanofi-aventis and Procter & Gamble). Clinical trial costs are dependent, among other things, on the size and duration of trials, fees charged for services provided by clinical trial investigators and other third parties, the costs for manufacturing the product candidate for use in the trials, supplies, laboratory tests, and other expenses. The amount of funding that will be required for our clinical programs depends upon the results of our research and preclinical programs and early-stage clinical trials, regulatory requirements, the clinical trials underway plus additional clinical trials that we decide to initiate, and the various factors that affect the cost of each trial as described above. In the future, if we are able to successfully develop, market, and sell certain of our product candidates, we may be required to pay royalties or otherwise share the profits generated on such sales in connection with our collaboration and licensing agreements. Also under the terms of the sanofi-aventis collaboration agreement, if the collaboration becomes profitable, we will reimburse sanofi-aventis for 50 percent of the VEGF Trap development expenses, including 50% of the $25.0 million payment received in connection with amending our collaboration agreement in January 2005, 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 addition, if the first commercial sale of a VEGF Trap product for diseases of the eye through local delivery systems predates the first commercial sale of a VEGF Trap product under the collaboration, we will begin reimbursing sanofi-aventis for up to $7.5 million of VEGF Trap development expenses commencing two years after such initial commercialization outside the collaboration in accordance with a formula until the first commercial VEGF Trap sale under the collaboration occurs. Sanofi-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 sanofi-aventis for 50% of the VEGF Trap development expenses will terminate and we will retain all rights to the VEGF Trap.

We expect that expenses related to the filing, prosecution, defense, and enforcement of patent and other intellectual property claims will continue to be substantial as a result of patent filings and prosecutions in the United States and foreign countries.

We believe that our existing capital resources will enable us to meet operating needs through at least mid-2007. However, this is a forward-looking statement based on our current operating plan, and there may be a change in projected revenues or expenses that would lead to our capital being consumed significantly before such time. If there is insufficient capital to fund all of our planned operations and activities, we believe we would prioritize available capital to fund preclinical and clinical development of our product candidates. We

have no off-balance sheet arrangements and do not guarantee the obligations of any other entity. As of December 31, 2004, we had no established banking arrangements through which we could obtain short-term financing or a line of credit. In the event we need additional financing for the operation of our business, we will consider collaborative arrangements and additional public or private financing, including additional equity financing. In January 2005, we filed a shelf registration statement on Form S-3 to sell, in one or more offerings, up to $200.0 million of equity or debt securities, together or separately, which registration statement was declared effective in February 2005. However, there is no assurance that we will be able to complete any such offerings of securities. Factors influencing the availability of additional financing include our progress in product development, investor perception of our prospects, and the general condition of the financial markets. We may not be able to secure the necessary funding through new collaborative arrangements or additional public or private offerings. If we cannot raise adequate funds to satisfy our capital requirements, we may have to delay, scale-back, or eliminate certain of our research and development activities or future operations. This could harm our business.

Critical Accounting Policies and Significant Judgments and Estimates

Revenue Recognition:

We recognize revenue from contract research and development and research progress payments in accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition* (SAB 104) and Emerging Issues Task Force 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables* (EITF 00-21). During the third quarter of 2003, we elected to change the method we use to recognize revenue under SAB 104 related to non-refundable collaborator payments, including up-front licensing payments, payments for development activities, and research progress (milestone) payments, to the Substantive Milestone Method, adopted retroactively to January 1, 2003. Under this method, we recognize revenue from non-refundable up-front license payments, not tied to achieving a specific performance milestone, ratably over the period over which we expect to perform services. The period over which we expect to perform services is estimated based on product development plans. These estimates are updated based on the results and progress of clinical trials and drug production and revisions to these estimates could result in changes to the amount of revenue recognized each year in the future. In addition, if a collaborator terminates the agreement in accordance with the terms of the contract, we would recognize the remainder of the up-front payment at the time of the termination. Payments for development activities are recognized as revenue as earned, ratably over the period of effort. Substantive at-risk milestone payments, which are based on achieving a specific performance milestone, are recognized as revenue when the milestone is achieved and the related payment is due, provided there is no future service obligation associated with that milestone. Previously, we had recognized revenue from non-refundable collaborator payments based on the percentage of costs incurred to date, estimated costs to complete, and total expected contract revenue. However, the revenue recognized was limited to the amount of non-refundable payments received. The change in accounting method was made because we believe that it better reflects the substance of our collaborative agreements and is more consistent with current practices in the biotechnology industry.

In connection with our VEGF Trap collaboration agreement with sanofi-aventis, in September 2003, we received a non-refundable up-front payment of $80.0 million which was recorded to deferred revenue and is being recognized as contract research and development revenue ratably over the period over which we are obligated to perform services. In the fourth quarter of 2004, we revised our estimate based on current VEGF Trap product development plans and extended the period over which we expect to be obligated to perform services under the collaboration by one year. As a result, we anticipate that we will recognize approximately $9.4 million of revenue related to the sanofi-aventis $80.0 million up-front payment over each of the next 7 years. Also, in connection with our collaboration agreement with Novartis, in the first quarter of 2004, Novartis provided notice of its intention not to proceed with the joint development of the IL-1 Trap. Accordingly, the remaining balance of the $27.0 million up-front payment, or $22.1 million, was recognized as contract research and development revenue.

Recognition of Deferred Revenue Related to Contract Manufacturing Agreement:

We have entered into a contract manufacturing agreement with Merck under which we manufacture a vaccine intermediate at our Rensselaer, New York facility and perform services. We recognize contract manufacturing revenue from this agreement after the product is tested and approved by, and shipped (FOB Shipping Point) to, Merck, and as services are performed. In connection with the agreement, we agreed to modify portions of our Rensselaer facility to manufacture Merck's vaccine intermediate and Merck agreed to reimburse us for the related capital costs. These capital cost payments were deferred and are recognized as revenue as product is shipped to Merck, based upon our estimate of Merck's order quantities each year through the expected end of the agreement which, for 2004 and prior years, was October 2005. Since we commenced production of the vaccine intermediate in November 1999, our estimates of Merck's order quantities each year have not been materially different from Merck's actual orders.

In February 2005, we and Merck amended our contract manufacturing agreement by extending its term by one year through October 2006. In addition, we provided Merck the opportunity, upon twelve months' prior notice, to extend the agreement for an additional year through October 2007. As a result, we will recognize the remaining deferred balance of Merck's capital cost payments as of December 31, 2004, or $2.7 million, as revenue as product is shipped to Merck, based upon our revised estimate of Merck's order quantities through October 2006.

Clinical Trial Accrual Estimates:

For each clinical trial that we conduct, certain clinical trial costs, which are included in research and development expenses, are expensed based on the expected total number of patients in the trial, the rate at which patients enter the trial, and the period over which clinical investigators or contract research organizations are expected to provide services. We believe that this method best aligns the expenses we record with the efforts we expend on a clinical trial. During the course of a trial, we adjust our rate of clinical expense recognition if actual results differ from our estimates. No material adjustments to our past clinical trial accrual estimates were made during the years ended December 31, 2004, 2003, and 2002.

Depreciation of Property, Plant and Equipment:

Property, plant, and equipment are stated at cost. Depreciation is provided on a straight-line basis over the estimated useful lives of the assets. Expenditures for maintenance and repairs which do not materially extend the useful lives of the assets are charged to expense as incurred. The cost and accumulated depreciation or amortization of assets retired or sold are removed from the respective accounts, and any gain or loss is recognized in operations. The estimated useful lives of property, plant, and equipment are as follows:

Building and improvements	6-30 years
Leasehold improvements	Life of lease
Laboratory and computer equipment	3-5 years
Furniture and fixtures	5 years

In some situations, the life of the asset may be extended or shortened if circumstances arise that would lead us to believe that the estimated life of the asset has changed. The life of leasehold improvements may change based on the extension of lease contracts with our landlords. Changes in the estimated lives of assets will result in an increase or decrease in the amount of depreciation recognized in future periods. Costs of construction of certain long-lived assets include capitalized interest which is amortized over the estimated useful life of the related asset.

Future Impact of Recently Issued Accounting Standards

In April 2004, the Emerging Issues Task Force issued Statement No. 03-6, *Participating Securities and the Two — Class Method under FASB Statement No. 128, Earnings per Share* (EITF 03-6). EITF 03-6 addresses a number of questions regarding the computation of earnings per share (EPS) by companies that have issued securities other than common stock that contractually entitle the holder to participate in dividends

and earnings of the company when, and if, it declares dividends on its common stock. EITF 03-6 defines participation rights based solely on whether the holder would be entitled to receive any dividends if the entity declared them during the period and requires the use of the two-class method for computing basic EPS when participating convertible securities exist. In addition, EITF 03-6 expands the use of the two-class method to encompass other forms of participating securities and is effective for fiscal periods beginning after March 31, 2004. Since we have no participating securities, our adoption of EITF 03-6 did not have a material impact on our financial statements.

In November 2004, the Financial Accounting Standards Board (FASB) issued Statement of Financial Accounting Standards No. 151, *Inventory Costs, an amendment of ARB 43, Chapter 4* (SFAS No. 151). SFAS No. 151 clarifies the accounting for abnormal amounts of idle facility expense, freight, handling costs, and wasted material by requiring that those items be recognized as current-period charges in all circumstances. SFAS No. 151 is effective for fiscal years beginning after June 15, 2005. We believe that the future adoption of SFAS No. 151 will not have a material impact on our financial statements.

In December 2004, the FASB issued Statement of Financial Accounting Standards No. 123R, *Share-Based Payment* (SFAS No. 123R). SFAS No. 123R is a revision of SFAS No. 123, *Accounting for Stock-Based Compensation*, and supersedes APB Opinion No. 25, *Accounting for Stock Issued to Employees*, and its related implementation guidance. SFAS No. 123R establishes standards for the accounting for transactions in which an entity exchanges its equity instruments for goods or services. SFAS No. 123R focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions, and requires the recognition of compensation expense in an amount equal to the fair value of the share-based payment (including stock options and restricted stock) issued to employees. SFAS No. 123R is effective for fiscal periods beginning after June 15, 2005. We currently intend to adopt SFAS No. 123R effective July 1, 2005 using the modified prospective method. Under the modified prospective method, compensation cost is recognized beginning with the effective date based on (a) the requirements of SFAS No. 123R for all share-based payments granted after the effective date and (b) the requirements of SFAS No. 123 for all awards granted to employees prior to the effective date of SFAS No. 123R that remain unvested on the effective date. Although the impact of adopting SFAS No. 123R has not yet been quantified, we believe that the future adoption of this standard will have a material impact on our financial statements.

In December 2004, the FASB issued Statement of Financial Accounting Standards No. 153, *Exchanges of Nonmonetary Assets, an amendment of APB Opinion No. 29* (SFAS No. 153). SFAS No. 153 eliminates an exception for nonmonetary exchanges of similar productive assets under APB Opinion No. 29, and replaces it with a general exception for exchanges of nonmonetary assets that do not have commercial substance. SFAS No. 153 is to be applied prospectively and is effective for nonmonetary asset exchanges occurring in fiscal periods beginning after June 15, 2005. We believe that the future adoption of SFAS No. 153 will not have a material impact on our financial statements.

Risk Factors

We operate in an environment that involves a number of significant risks and uncertainties. We caution you to read the following risk factors, which have affected, and/or in the future could affect, our business, operating results, financial condition, and cash flows. The risks described below include forward-looking statements, and actual events and our actual results may differ substantially from those discussed in these forward-looking statements. Additional risks and uncertainties not currently known to us or that we currently deem immaterial may also impair our business operations. Furthermore, additional risks and uncertainties are discussed elsewhere in this Annual Report on Form 10-K and should be considered by our investors.

Risks Related to Our Financial Results and Need for Additional Financing

We have had a history of operating losses and we may never achieve profitability. If we continue to incur operating losses, we may be unable to continue our operations.

From inception on January 8, 1988 through December 31, 2004, we had a cumulative loss of $489.8 million. If we continue to incur operating losses and fail to become a profitable company, we may be

unable to continue our operations. We have no products that are available for sale and do not know when we will have products available for sale, if ever. In the absence of revenue from the sale of products or other sources, the amount, timing, nature or source of which cannot be predicted, our losses will continue as we conduct our research and development activities. We currently receive contract manufacturing revenue from our agreement with Merck and contract research and development revenue from our agreements with Procter & Gamble and Serono. Our agreements with Procter & Gamble and Serono may expire in 2005. Our agreement with Merck is scheduled to expire before the end of 2006, unless extended for one additional year by Merck. We can provide no assurance that all or any of these agreements will be extended. Failure to extend these agreements may negatively impact our business, financial condition or results of operations.

We will need additional funding in the future, which may not be available to us, and which may force us to delay, reduce or eliminate our product development programs or commercialization efforts.

We will need to expend substantial resources for research and development, including costs associated with clinical testing of our product candidates. We believe our existing capital resources will enable us to meet operating needs through at least mid-2007; however, our projected revenue may decrease or our expenses may increase and that would lead to our capital being consumed significantly before such time. We will likely require additional financing in the future and we may not be able to raise such additional funds. If we are able to obtain additional financing through the sale of equity or convertible debt securities, such sales may be dilutive to our shareholders. Debt financing arrangements may require us to pledge certain assets or enter into covenants that would restrict our business activities or our ability to incur further indebtedness and may contain other terms that are not favorable to our shareholders. If we are unable to raise sufficient funds to complete the development of our product candidates, we may face delay, reduction or elimination of our research and development programs or preclinical or clinical trials, in which case our business, financial condition or results of operations may be materially harmed.

We have a significant amount of debt and may have insufficient cash to satisfy our debt service and repayment obligations. In addition, the amount of our debt could impede our operations and flexibility.

We have a significant amount of convertible debt and semi-annual interest payment obligations. This debt, unless converted to shares of our common stock, will mature in October 2008. We may be unable to generate sufficient cash flow or otherwise obtain funds necessary to make required payments on our debt. Even if we are able to meet our debt service obligations, the amount of debt we already have could hurt our ability to obtain any necessary financing in the future for working capital, capital expenditures, debt service requirements or other purposes. In addition, our debt obligations could require us to use a substantial portion of cash to pay principal and interest on our debt, instead of applying those funds to other purposes, such as research and development, working capital, and capital expenditures.

We intend to adopt, effective January 1, 2005, the fair market value based method of accounting for stock-based employee compensation. This is expected to materially increase our non-cash compensation expenses in our Statement of Operations commencing in 2005, primarily due to compensation costs related to stock options.

We intend to adopt, effective January 1, 2005, the fair value based method of accounting for stock-based employee compensation under the provisions of SFAS Statement of Financial Accounting Standards No. 123 (SFAS No. 123), *Accounting for Stock Based Compensation*, as modified by Statement of Accounting Standards No. 148 (SFAS No. 148), *Accounting for Stock Based Compensation — Transition and Disclosure*, using the modified prospective method. SFAS Nos. 123/148 require that compensation expense in an amount equal to the fair market value of the share-based payment (including stock option awards) be recognized over the vesting period of the awards. We expect to begin recognizing this compensation cost in the first quarter of 2005. The impact of adopting SFAS Nos. 123/148 in 2005 has not yet been quantified. However, had we adopted SFAS Nos. 123/148 effective January 1, 2004, our net income would have decreased by approximately $33.6 million and our basic net income per share would have decreased from $0.75 per share to $0.15 per share.

In addition, in December 2004, the FASB issued SFAS No. 123R, *Share-Based Payment*, which is a revision of SFAS No. 123 and supersedes APB Opinion No. 25, *Accounting for Stock Issued to Employees.* SFAS No. 123R requires the recognition of compensation expense in an amount equal to the fair value of share-based payments (including stock options) issued to employees. We will be required to adopt SFAS No. 123R effective for the quarter beginning July 1, 2005. The impact of adopting SFAS No. 123R has not yet been quantified.

The expected negative impact on our income (loss) as a result of adopting SFAS No. 123/148 commencing January 1, 2005, and subsequently adopting SFAS No. 123R commencing July 1, 2005, may materially negatively affect our stock price.

Risks Related to Development of Our Product Candidates

Successful development of any of our product candidates is highly uncertain.

Only a small minority of all research and development programs ultimately result in commercially successful drugs. We have never developed a drug that has been approved for marketing and sale, and we may never succeed in developing an approved drug. Even if clinical trials demonstrate safety and effectiveness of any of our product candidates for a specific disease 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 and our partners' ability to successfully manufacture and commercialize our product candidates. Our product candidates are delivered either by intravenous, intravitreal or subcutaneous injections, which are generally less well received by patients than tablet or capsule delivery. If our products are not successfully commercialized, we will not be able to recover the significant investment we have made in developing such products and our business would be severely harmed.

Clinical trials required for our product candidates are expensive and time-consuming, and their outcome is highly uncertain. If any of our drug trials are delayed or achieve unfavorable results, we will have to delay or may be unable to obtain regulatory approval for our product candidates.

We must conduct extensive testing of our product candidates before we can obtain regulatory approval to market and sell them. We need to conduct both preclinical animal testing and human clinical trials. Conducting these trials is a lengthy, time-consuming, and expensive process. These tests and trials may not achieve favorable results for many reasons, including, among others, failure of the product candidate to demonstrate safety or efficacy, the development of serious or life-threatening adverse events (or side effects) caused by or connected with exposure to the product candidate, difficulty in enrolling and maintaining subjects in the clinical trial, lack of sufficient supplies of the product candidate, and the failure of clinical investigators, trial monitors and other consultants, or trial subjects to comply with the trial plan or protocol. A clinical trial may fail because it did not include a sufficient number of patients to detect the endpoint being measured or reach statistical significance. A clinical trial may also fail because the dose(s) of the investigational drug included in the trial were either too low or too high to determine the optimal effect of the investigational drug in the disease setting. For example, we intend to study higher doses of the IL-1 Trap after a previous phase 2 trial of the IL-1 Trap in subjects with rheumatoid arthritis failed to achieve its primary endpoint. Additional clinical trial risks and examples of our prior clinical trials which did not achieve favorable results are described in the risk factor below entitled "*A previous phase 3 study evaluating AXOKINE demonstrated modest average weight loss over a 12-month period. In addition, a completed phase 2 study evaluating the IL-1 Trap in patients with rheumatoid arthritis failed to achieve its primary endpoint.*"

We will need to reevaluate any drug candidate that does not test favorably and either conduct new trials, which are expensive and time consuming, or abandon the drug development program. Even if we obtain positive results from preclinical or clinical trials, we may not achieve the same success in future trials. Many companies in the biopharmaceutical industry, including us, have suffered significant setbacks in clinical trials, even after promising results have been obtained in earlier trials. The failure of clinical trials to demonstrate safety and effectiveness for the desired indication(s) could harm the development of the product candidate(s), and our business, financial condition, and results of operations may be materially harmed.

The development of serious or life-threatening side effects with any of our product candidates would lead to delay or discontinuation of development, which could severely harm our business.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the drug candidate being studied caused these conditions. Various illnesses, injuries, and discomforts have been reported from time-to-time during clinical trials of our product candidates. Although our current drug candidates appeared to be generally well tolerated in clinical trials conducted to date, it is possible as we test any of them in larger, longer, and more extensive clinical programs, illnesses, injuries, and discomforts that were observed in earlier trials, as well as conditions that did not occur or went undetected in smaller previous trials, will be reported by patients. Many times, side effects are only detectable after investigational drugs are tested in large scale, phase 3 clinical trials or, in some cases, after they are made available to patients after approval. If additional clinical experience indicates that any of our product candidates has many side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, which would severely harm our business.

Our VEGF Trap is being studied for the potential treatment of certain types of cancer and diseases of the eye. There are many potential safety concerns associated with significant blockade of vascular endothelial growth factor, or VEGF. These risks, based on the clinical and preclinical experience of systemically delivered VEGF inhibitors, including the VEGF Trap, include bleeding, hypertension, and proteinuria. These serious side effects and other serious side effects have been reported in our VEGF Trap studies in cancer and diseases of the eye. In addition, patients given infusions of any protein, including the VEGF Trap delivered through intravenous administration, may develop severe hypersensitivity reactions, referred to as infusion reactions. These and other complications or side effects could harm the development of the VEGF Trap for either the treatment of cancer or diseases of the eye.

Although the IL-1 Trap was generally well tolerated and was not associated with any drug-related serious adverse events in the phase 2 rheumatoid arthritis study completed in 2003, safety or tolerability concerns may arise as we test higher doses of the IL-1 Trap in patients with rheumatoid arthritis and other inflammatory diseases and disorders. Like TNF-antagonists such as Enbrel® (a registered trademark of Amgen) and Remicade® (a registered trademark of Centocor), the IL-1 Trap affects the immune defense system of the body by blocking some of its functions. Therefore, there may be an increased risk for infections to develop in patients treated with the IL-1 Trap. In addition, patients given infusions of the IL-1 Trap delivered through intravenous administration have developed hypersensitivity reactions, referred to as infusion reactions. These and other complications or side effects could harm the development of the IL-1 Trap.

Our product candidates in development are recombinant proteins that could cause an immune response, resulting in the creation of harmful or neutralizing antibodies against the therapeutic protein.

In addition to the safety, efficacy, manufacturing, and regulatory hurdles faced by our product candidates, the administration of recombinant proteins frequently causes an immune response, resulting in the creation of antibodies against the therapeutic protein. The antibodies can have no effect or can totally neutralize the effectiveness of the protein, or require that higher doses be used to obtain a therapeutic effect. In some cases, the antibody can cross react with the patient's own proteins, resulting in an "auto-immune" type disease. Whether antibodies will be created can often not be predicted from preclinical or clinical experiments, and their appearance is often delayed, so that there can be no assurance that neutralizing antibodies will not be created at a later date — in some cases even after pivotal clinical trials have been completed. Approximately two-thirds of the subjects who received AXOKINE in the completed phase 3 study developed neutralizing antibodies. In addition, subjects who received the IL-1 Trap in clinical trials have developed antibodies. It is possible that as we test the VEGF Trap in different patient populations and larger clinical trials, subjects given the VEGF Trap will develop antibodies to the product candidate.

A previous phase 3 study evaluating AXOKINE demonstrated modest average weight loss over a 12-month period. In addition, a completed phase 2 study evaluating the IL-1 Trap in patients with rheumatoid arthritis failed to achieve its primary endpoint.

In March 2003, we reported data from the 12-month treatment period of our initial phase 3 pivotal trial of AXOKINE. Although the phase 3 study met its primary endpoints and individuals achieved a medically meaningful weight loss, the average weight loss was small and limited by the development of antibodies.

In October 2003, we reported results from the first phase 2 trial of our IL-1 Trap in rheumatoid arthritis. We plan to conduct large-scale rheumatoid arthritis trials of the IL-1 Trap in a larger patient population, testing higher doses than were tested in the previous phase 2 trial for a longer period of time. We plan to study higher doses of the IL-1 Trap through subcutaneous injections and intravenous delivery. However, higher doses may not lead to better results than were demonstrated in the previous phase 2 trial. In addition, safety or tolerability concerns may arise which limit our ability to deliver higher doses of the IL-1 Trap to patients. The dose levels that will be tested are substantially higher than the dose levels of other biological therapeutics currently approved for the treatment of rheumatoid arthritis. The higher doses may affect the safety and/or tolerability of the IL-1 Trap, which may limit its commercial potential if the product candidate is ever approved for marketing and sale.

We intend to study our lead product candidates, the VEGF Trap and IL-1 Trap, in a wide variety of indications in so-called “proof of concept” studies. We intend to study the VEGF Trap in a variety of cancer settings and ophthalmologic indications and the IL-1 Trap in a wide variety of inflammatory disorders. The specific indications were selected based on available pre-clinical and clinical data from medical publications, our product candidates, and competitive agents. The purpose of these exploratory “proof of concept” studies is to identify what diseases, if any, are best suited for treatment with these product candidates. However, it is likely that our product candidates will not demonstrate the requisite efficacy and/or safety profile to support continued development for most of the indications that are to be studied in these “proof of concepts” studies. In fact, our product candidates may not demonstrate the requisite efficacy and safety profile to support the continued development for any of the indications studied in these early-stage trials.

Regulatory and Litigation Risks

If we do not obtain regulatory approval for our product candidates, we will not be able to market or sell them.

We cannot sell or market products without regulatory approval. If we do not obtain and maintain regulatory approval for our product candidates, the value of our company and our results of operations will be harmed. In the United States, we must obtain and maintain approval from the United States Food and Drug Administration (FDA) for each drug we intend to sell. Obtaining FDA approval is typically a lengthy and expensive process, and approval is highly uncertain. Foreign governments also regulate drugs distributed in their country and approval in any country is likely to be a lengthy and expensive process, and approval is highly uncertain. None of our product candidates has ever received regulatory approval to be marketed and sold in the United States or any other country. We may never receive regulatory approval for any of our product candidates.

If the testing or use of our products harms people, we could be subject to costly and damaging product liability claims. We could also face costly and damaging claims arising from employment law, securities law, environmental law or other applicable laws governing our operations.

The testing, manufacturing, marketing, and sale of drugs for use in people expose us to product liability risk. We are currently involved in a product liability lawsuit brought by a subject who participated in a clinical trial of one of our drug candidates. Any informed consent or waivers obtained from people who sign up for our clinical trials may not protect us from liability or the cost of litigation. Our product liability insurance may not cover all potential liabilities or may not completely cover any liability arising from any such litigation. Moreover, we may not have access to liability insurance or be able to maintain our insurance on acceptable terms.

In May 2003, purported class action securities lawsuits were commenced against us and certain of our 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. On February 1, 2005, the United States District Court of the Southern District for New York denied our motion to dismiss the consolidated amended complaint. We believe the lawsuit is without merit and intend to continue to defend the action vigorously. Because we do not believe that a loss is probable, no legal reserve has been established. However, we cannot assure investors that we will be successful in defending this action, or that the amount of any settlement or judgment in this action will not exceed the coverage limits of our director and officers liability insurance policies. If we are not successful in defending this action, our business and financial condition could be adversely affected. In addition, whether or not we are successful, the defense of this action may divert attention of our management and other resources that would otherwise be engaged in running our business.

Our operations may involve hazardous materials and are subject to environmental, health, and safety laws and regulations. We may incur substantial liability arising from our activities involving the use of hazardous materials.

As a biopharmaceutical company with significant manufacturing operations, we are subject to extensive environmental, health, and safety laws and regulations, including those governing the use of hazardous materials. Our research and development and manufacturing activities involve the controlled use of chemicals, viruses, radioactive compounds, and other hazardous materials. The cost of compliance with environmental, health, and safety regulations is substantial. If an accident involving these materials or an environmental discharge were to occur, we could be held liable for any resulting damages, or face regulatory actions, which could exceed our resources or insurance coverage.

Risks Related to Our Dependence on Third Parties

On February 27, 2004, Novartis Pharma AG provided notice to us that they would not participate in the continued development and commercialization of the IL-1 Trap under our collaboration agreement. This may harm our ability to develop and commercialize the IL-1 Trap.

We relied heavily on Novartis to provide their expertise, resources, funding, manufacturing capacity, clinical expertise, and commercial infrastructure to support the IL-1 Trap program. Novartis' decision to withdraw from participating in the development and commercialization of the IL-1 Trap may delay or disrupt the IL-1 Trap program. We do not have the resources and skills to replace those of Novartis, which could result in significant delays in the development and potential commercialization of the IL-1 Trap. In addition, we will have to fund the development and commercialization of the IL-1 Trap without Novartis' long-term commitment, which will require substantially greater expenditures on our part.

If our collaboration with sanofi-aventis for the VEGF Trap is terminated, our business operations and our ability to develop, manufacture, and commercialize the VEGF Trap in the time expected, or at all, would be harmed.

We rely heavily on sanofi-aventis to assist with the development of the VEGF Trap. If the VEGF Trap program continues, we will rely on sanofi-aventis to assist with funding the VEGF Trap program, providing commercial manufacturing capacity, enrolling and monitoring clinical trials, obtaining regulatory approval, particularly outside the United States, and providing sales and marketing support. While we cannot assure you that the VEGF Trap will ever be successfully developed and commercialized, if sanofi-aventis does not perform its obligations in a timely manner, or at all, our ability to develop, manufacture, and commercialize the VEGF Trap will be significantly adversely affected. Sanofi-aventis has the right to terminate its collaboration agreement with us at any time. If sanofi-aventis were to terminate its collaboration agreement

with us, we might not have the resources or skills to replace those of our partner, which could cause significant delays in the development and/or manufacture of the VEGF Trap and result in substantial additional costs to us. We have no sales, marketing or distribution capabilities and would have to develop or outsource these capabilities. Termination of the sanofi-aventis collaboration agreement would create new and additional risks to the successful development of the VEGF Trap.

Our collaborators and service providers may fail to perform adequately in their efforts to support the development, manufacture, and commercialization of our drug candidates.

We depend upon third-party collaborators, including sanofi-aventis and service providers such as clinical research organizations, outside testing laboratories, clinical investigator sites, and third party manufacturers and product packagers and labelers, to assist us in the development of our product candidates. If any of our existing collaborators or service providers breaches or terminates its agreement with us or does not perform its development or manufacturing services under an agreement in a timely manner or at all, we would experience additional costs, delays, and difficulties in the development or ultimate commercialization of our product candidates.

Risks Related to the Manufacture of Our Product Candidates

We have limited manufacturing capacity, which could inhibit our ability to successfully develop or commercialize our drugs.

Before approving a new drug or biologic product, the FDA requires that the facilities at which the product will be manufactured be in compliance with current good manufacturing practices, or cGMP requirements. Manufacturing product candidates in compliance with these regulatory requirements is complex, time-consuming, and expensive. To be successful, our products must be manufactured for development, following approval, in commercial quantities, in compliance with regulatory requirements, and at competitive costs. If we or any of our product collaborators or third-party manufacturers, fillers or labelers are unable to maintain regulatory compliance, the FDA can impose regulatory sanctions, including, among other things, refusal to approve a pending application for a new drug or biologic product, or revocation of a pre-existing approval. As a result, our business, financial condition, and results of operations may be materially harmed.

Our manufacturing facility is likely to be inadequate to produce sufficient quantities of product for commercial sale. We intend to rely on our corporate collaborators, as well as contract manufacturers, to produce the large quantities of drug material needed for commercialization of our products. We rely entirely on third party manufacturers for filling and finishing services. We will have to depend on these manufacturers to deliver material on a timely basis and to comply with regulatory requirements. If we are unable to supply sufficient material on acceptable terms, or if we should encounter delays or difficulties in our relationships with our corporate collaborators or contract manufacturers, our business, financial condition, and results of operations may be materially harmed.

We may expand our own manufacturing capacity to support commercial production of active pharmaceutical ingredients, or API, for our product candidates. This will require substantial additional funds, and we will need to hire and train significant numbers of employees and managerial personnel to staff our facility. Start-up costs can be large and scale-up entails significant risks related to process development and manufacturing yields. We may be unable to develop manufacturing facilities that are sufficient to produce drug material for clinical trials or commercial use. In addition, we may be unable to secure adequate filling and finishing services to support our products. As a result, our business, financial condition, and results of operations may be materially harmed.

We may be unable to obtain key raw materials and supplies for the manufacture of our product candidates. In addition, we may face difficulties in developing or acquiring production technology and managerial personnel to manufacture sufficient quantities of our product candidates at reasonable costs and in compliance with applicable quality assurance and environmental regulations and governmental permitting requirements.

If any of our clinical programs are discontinued, we may face costs related to the unused capacity at our manufacturing facilities.

We have large-scale manufacturing operations in Rensselaer, New York. Under a long-term manufacturing agreement with Merck, which expires in October 2006 unless extended for one additional year by Merck, we produce an intermediate for a Merck pediatric vaccine at our facility in Rensselaer, New York. We also use our facilities to produce API for our own clinical and preclinical candidates. If we no longer use our facilities to manufacture the Merck intermediate or clinical candidates are discontinued, we would have to absorb overhead costs and inefficiencies.

Certain of our raw materials are single-sourced from third parties; third-party supply failures could adversely affect our ability to supply our products.

Certain raw materials necessary for manufacturing and formulation of our product candidates are provided by single-source unaffiliated third-party suppliers. We would be unable to obtain these raw materials for an indeterminate period of time if these third-party single-source suppliers were to cease or interrupt production or otherwise fail to supply these materials or products to us for any reason, including due to regulatory requirements or action, due to adverse financial developments at or affecting the supplier or due to labor shortages or disputes. This, in turn, could materially and adversely affect our ability to manufacture our product candidates for use in clinical trials, which could materially and adversely affect our business and future prospects.

Also, certain of the raw materials required in the manufacturing and the formulation of our clinical candidates may be derived from biological sources, including mammalian tissues, bovine serum, and human serum albumin. There are certain European regulatory restrictions on using these biological source materials. If we are required to substitute these sources to comply with European regulatory requirements, our clinical development activities may be delayed or interrupted.

Risks Related to Commercialization of Products

If we are unable to establish sales, marketing, and distribution capabilities, or enter into agreements with third parties to do so, we will be unable to successfully market and sell future products.

We have no sales or distribution personnel or capabilities and have only a small staff with marketing capabilities. If we are unable to obtain those capabilities, either by developing our own organizations or entering into agreements with service providers, we will not be able to successfully sell any products that we may obtain regulatory approval for and bring to market in the future. In that event, we will not be able to generate significant revenue, even if our product candidates are approved. We cannot guarantee that we will be able to hire the qualified sales and marketing personnel we need or that we will be able to enter into marketing or distribution agreements with third-party providers on acceptable terms, if at all. Under the terms of our collaboration agreement with sanofi-aventis, we currently rely on sanofi-aventis for sales, marketing, and distribution of the VEGF Trap, should it be approved in the future by regulatory authorities for marketing. We will have to rely on a third party or devote significant resources to develop our own sales, marketing, and distribution capabilities for our other product candidates, and we may be unsuccessful in developing our own sales, marketing, and distribution organization.

We may be unable to formulate or manufacture our product candidates in a way that is suitable for clinical or commercial use.

Changes in product formulations and manufacturing processes may be required as product candidates progress in clinical development and are ultimately commercialized. If we are unable to develop suitable product formulations or manufacturing processes to support large scale clinical testing of our product candidates, including the VEGF Trap, IL-1 Trap, and IL-4/13 Trap, we may be unable to supply necessary materials for our clinical trials, which would delay the development of our product candidates. Similarly, if we are unable to supply sufficient quantities of our product or develop product formulations suitable for commercial use, we will not be able to successfully commercialize our product candidates. For example, we

are in the process of developing formulations that would allow delivery of higher doses of the IL-1 Trap to test in clinical trials. The dose levels that will be tested are substantially higher than the dose levels of other biological therapeutics currently approved for treatment of rheumatoid arthritis. Separate new formulations will be used for subcutaneous and intravenous administration of the higher dose therapeutic. If we are unable to develop or manufacture such a higher dose formulation that can be produced in a cost-effective manner, potential future IL-1 Trap sales and profitability may be limited.

Even if our product candidates are ever approved, their commercial success is highly uncertain because our competitors may get to the marketplace before we do with better or lower cost drugs or the market for our product candidates may be too small to support commercialization or sufficient profitability.

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 enhance their competitive position if they acquire or discover patentable inventions, form collaborative arrangements or merge with large pharmaceutical companies. Even if we achieve product commercialization, our competitors have achieved, and may continue to achieve, product commercialization before our products are approved for marketing and sale.

Genentech has an approved VEGF antagonist on the market for treating certain cancers and many different pharmaceutical and biotechnology companies are working to develop competing VEGF antagonists, including Novartis, Eyetech Pharmaceuticals, and Pfizer. Many of these molecules are further along in development than the VEGF Trap and may offer competitive advantages over our molecule. Novartis has an ongoing phase 3 clinical development program evaluating an orally delivered VEGF tyrosine kinase in different cancer settings. If this phase 3 product candidate is safer and more efficacious than Genentech's approved VEGF antibody in these cancer settings, it will make it more difficult for us to successfully develop and commercialize the VEGF Trap. The marketing approval for Genentech's VEGF antagonist, Avastin™, may make it more difficult for us to enroll patients in clinical trials to support the VEGF Trap and to obtain regulatory approval of the VEGF Trap in these cancer settings. This may delay or impair our ability to successfully develop and commercialize the VEGF Trap. In addition, even if the VEGF Trap is ever approved for sale for the treatment of certain cancers, it will be difficult for our drug to compete against Avastin and, if approved by the FDA, the Novartis phase 3 tyrosine kinase, because doctors and patients will have significant experience using these medicines.

The market for eye diseases is also very competitive. Eyetech Pharmaceuticals and Pfizer are marketing an approved VEGF inhibitor for age-related macular degeneration. Novartis and Genentech are collaborating on another VEGF inhibitor for the treatment of eye diseases that is in phase 3 development. The marketing approval of the Eyetech/ Pfizer VEGF inhibitor and the potential approval of the Novarits/ Genentech VEGF antibody makes it more difficult for us to successfully develop the VEGF Trap in eye diseases. In addition, even if the VEGF Trap is ever approved for sale for the treatment of eye diseases, it will be difficult for our drug to compete against the Eyetech/ Pfizer drug and, if approved by the FDA, the Novartis/ Genentech phase 3 VEGF antibody, because doctors and patients will have significant experience using these medicines.

The markets for both rheumatoid arthritis and asthma are both very competitive. Several 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 Laboratories) for rheumatoid arthritis, the IL-1 receptor antagonist Kineret® (a registered trademark of Amgen), 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 and other marketed therapies makes it more difficult to successfully develop the IL-1 Trap for the treatment of rheumatoid arthritis, since it will be difficult to enroll patients with rheumatoid arthritis to participate in clinical trials of the IL-1 Trap. This 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. Moreover, these approved therapeutics may

offer competitive advantages over the IL-1 Trap, such as requiring fewer injections. In addition, there are both small molecules and antibodies in development by third parties that are designed to block the synthesis of interleukin-1 or inhibit the signaling of interleukin-1. For example, Vertex Pharmaceuticals Incorporated is developing an oral cytokine inhibitor of interleukin-1 beta converting enzyme (ICE). These drug candidates could offer competitive advantages over the IL-1 Trap. The successful development of these competing molecules could delay or impair our ability to successfully develop and commercialize the IL-1 Trap.

We are developing the IL-1 Trap for the treatment of a spectrum of rare diseases associated with mutations in the *CIAS1* gene. These rare genetic disorders affect a small group of people, estimated to be between several hundred and a few thousand. There may be too few patients with these genetic disorders to profitably commercialize the IL-1 Trap in this indication.

The successful commercialization of our product candidates will depend on obtaining coverage and reimbursement for use of these products from third-party payors.

Sales of biopharmaceutical products largely depend on the reimbursement of patients' medical expenses by government health care programs and private health insurers. Without the financial support of the governments or third-party payors, the market for any biopharmaceutical product will be limited. These third-party payors increasingly challenge the price and examine the cost-effectiveness of products and services. Significant uncertainty exists as to the reimbursement status of any new therapeutic, particularly if there exist lower-cost standards of care. Third-party payors may not reimburse sales of our products, which would harm our business.

Risk Related to Employees

We are dependent on our key personnel and if we cannot recruit and retain leaders in our research, development, manufacturing, and commercial organizations, our business will be harmed.

We are highly dependent on our executive officers. If we are not able to retain any of these persons or our Chairman, our business may suffer. In particular, we depend on the services of Roy Vagelos, M.D., the Chairman of our Board of Directors, Leonard Schleifer, M.D., Ph.D., our President and Chief Executive Officer, and George D. Yancopoulos, M.D., Ph.D., our Executive Vice President, Chief Scientific Officer and President, Regeneron Research Laboratories. There is intense competition in the biotechnology industry for qualified scientists and managerial personnel in the development, manufacture, and commercialization of drugs. We may not be able to continue to attract and retain the qualified personnel necessary for developing our business.

Risks Related to Intellectual Property

If we cannot protect the confidentiality of our trade secrets or our patents are insufficient to protect our proprietary rights, our business and competitive position will be harmed.

Our business requires using sensitive and proprietary technology and other information that we protect as trade secrets. We seek to prevent improper disclosure of these trade secrets through confidentiality agreements. If our trade secrets are improperly exposed, either by our own employees or our collaborators, it would help our competitors and adversely affect our business. We will be able to protect our proprietary rights from unauthorized use by third parties only to the extent that our rights are covered by valid and enforceable patents or are effectively maintained as trade secrets. The patent position of biotechnology companies involves complex legal and factual questions and, therefore, enforceability cannot be predicted with certainty. Our patents may be challenged, invalidated or circumvented. Patent applications filed outside the United States may be challenged by third parties who file an opposition. Such opposition proceedings are increasingly common in the European Union and are costly to defend. We have patent applications that are being opposed and it is likely that we will need to defend additional patent applications in the future. Our patent rights may not provide us with a proprietary position or competitive advantages against competitors. Furthermore, even if the outcome is favorable to us, the enforcement of our intellectual property rights can be expensive and time consuming.

We may be restricted in our development and/or commercialization activities by third party patents.

Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Other parties may allege that they have blocking patents to our Trap products in clinical development, either because they claim to hold proprietary rights to fusion proteins or proprietary rights to components of the Trap or the way it is manufactured. We are aware of certain United States and foreign patents relating to particular IL-4 and IL-13 receptors. Our IL-4/13 Trap includes portions of the IL-4 and IL-13 receptors. In addition, we are aware of a broad patent held by Genentech relating to proteins fused to certain immunoglobulin domains. Our Trap product candidates include proteins fused to immunoglobulin domains. Although we do not believe that we are infringing valid and enforceable third party patents, the holders of these patents may sue us for infringement and a court may find that we are infringing one or more validly issued patents, which may materially harm our business.

Any patent holders could sue us for damages and seek to prevent us from manufacturing, selling or developing our drug candidates, and a court may find that we are infringing validly issued patents of third parties. In the event that the manufacture, use or sale of any of our clinical candidates infringes on the patents or violates other proprietary rights of third parties, we may be prevented from pursuing product development, manufacturing, and commercialization of our drugs and may be required to pay costly damages. Such a result may materially harm our business, financial condition, and results of operations. Legal disputes are likely to be costly and time consuming to defend.

We seek to obtain licenses to patents when, in our judgment, such licenses are needed. If any licenses are required, we may not be able to obtain such licenses on commercially reasonable terms, if at all. The failure to obtain any such license could prevent us from developing or commercializing any one or more of our product candidates, which could severely harm our business.

Risks Related to Our Common Stock

Our stock price is extremely volatile.

There has been significant volatility in our stock price and generally in the market prices of biotechnology companies' securities. Various factors and events may have a significant impact on the market price of our common stock. These factors include, by way of example:

- progress, delays or adverse results in clinical trials;
- announcement of technological innovations or product candidates by us or competitors;
- fluctuations in our operating results;
- public concern as to the safety or effectiveness of our product candidates;
- developments in our relationship with collaborative partners;
- developments in the biotechnology industry or in government regulation of healthcare;
- large sales of our common stock by our executive officers, directors or significant shareholders;
- arrivals and departures of key personnel; and
- general market conditions.

The trading price of our common stock has been, and could continue to be, subject to wide fluctuations in response to these and other factors, including the sale or attempted sale of a large amount of our common stock in the market. Broad market fluctuations may also adversely affect the market price of our common stock.

Future sales of our common stock by our significant shareholders or us may depress our stock price and impair our ability to raise funds in new share offerings.

A small number of our shareholders beneficially own a substantial amount of our common stock. As of February 22, 2005, our seven largest shareholders, which include sanofi-aventis and Novartis, beneficially owned 54.5% of our outstanding shares of Common Stock and Class A stock, assuming, in the case of Leonard S. Schleifer, M.D., Ph.D, our chief executive officer, the exercise of all options held by him which are exercisable within 60 days of February 22, 2005. As of that date, Novartis owned 7,527,050 shares of Common Stock, representing approximately 13.4% of the shares of Common Stock and Class A stock then outstanding. Under our registration rights agreement with Novartis, these shares of Common Stock may generally not be sold or otherwise transferred by Novartis until after March 28, 2005. Commencing after March 28, 2005, Novartis has certain registration rights with respect to these shares. As of February 22, 2005, sanofi-aventis owned 2,799,552 shares of Common Stock, representing approximately 5.0% of the shares of Common Stock and Class A stock then outstanding. Under our stock purchase agreement with sanofi-aventis, these shares may generally not be sold or otherwise transferred until after September 5, 2005, and for one year after that date, sanofi-aventis may sell no more than 250,000 shares in any calendar quarter. After September 5, 2006, sanofi-aventis may sell no more than 500,000 shares in any calendar quarter. Accordingly, in 2005 and thereafter, as the restrictions on transfer applicable to the shares of Common Stock owned by Novartis and sanofi-aventis expire, these shares will be freely tradeable in the public market, subject, in the case of sanofi-aventis, to the foregoing continuing contractual sales volume restrictions. If Novartis or sanofi-aventis, or our other significant shareholders or we, sell substantial amounts of our Common Stock in the public market, or the perception that such sales may occur exists, the market price of our Common Stock could fall. Sales of Common Stock by our significant shareholders, including sanofi-aventis and Novartis, also might make it more difficult for us to raise funds by selling equity or equity-related securities in the future at a time and price that we deem appropriate.

Our existing shareholders may be able to exert significant influence over matters requiring shareholder approval.

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, while holders of Common Stock are entitled to one vote per share. As of February 22, 2005, holders of Class A stock held 4.2% of all shares of Common Stock and Class A stock then outstanding, and had 30.5% of the combined voting power of all shares of Common Stock and Class A stock. These shareholders, if acting together, would be in a position to significantly influence the election of our directors and to effect or prevent certain corporate transactions that require majority or supermajority approval of the combined classes, including mergers and other business combinations. This may result in our company taking corporate actions that you may not consider to be in your best interest and may affect the price of our common stock. As of February 22, 2005:

- our current officers and directors beneficially owned 13.3% of our outstanding shares of Common Stock and Class A stock and 33.4% of the combined voting power of our shares of Common Stock and Class A stock, assuming the exercise of all options held by such persons which are exercisable within 60 days of February 22, 2005; and
- our seven largest shareholders beneficially owned 54.5% of our outstanding shares of Common Stock and Class A stock and 60.1% of the combined voting power of our shares of Common Stock and Class A stock, assuming, in the case of Leonard S. Schleifer, M.D., Ph.D, our chief executive officer, the exercise of all options held by him which are exercisable within 60 days of February 22, 2005.

The anti-takeover effects of provisions of our charter, by-laws and our rights agreement, and of New York corporate law, could deter, delay or prevent an acquisition or other "change in control" of us and could adversely affect the price of our common stock.

Our amended and restated certificate of incorporation, our by-laws, our rights agreement and the New York Business Corporation Law contain various 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. Some of 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 those of our common shareholders;
- a staggered board of directors, so that it would take three successive annual meetings to replace all of our directors;
- a requirement that removal of directors may only be effected for cause and only upon the affirmative vote of at least eighty percent (80%) of the outstanding shares entitled to vote for directors, as well as a requirement that any vacancy on the board of directors may be filled only by the remaining directors;
- any action required or permitted to be taken at any meeting of shareholders may be taken without a meeting, only if, prior to such action, all of our shareholders consent, the effect of which is to require that shareholder action may only be taken at a duly convened meeting;
- any shareholder seeking to bring business before an annual meeting of shareholders must provide timely notice of this intention in writing and meet various other requirements; and
- under the New York Business Corporation Law, a plan of merger or consolidation of the Company must be approved by $^2/_3$ of the votes of all outstanding shares entitled to vote thereon. See the risk factor immediately above captioned *"Our existing shareholders may be able to exert significant influence over matters requiring shareholder approval."*

We have a shareholder rights plan which could make it more difficult for a third party to acquire us without the support of our board of directors and principal shareholders. In addition, many of our stock options issued under our 2000 Long-Term Incentive Plan may become fully vested in connection with a "change in control" of the Company, as defined in the plan.

Item 7A. ***Quantitative and Qualitative Disclosure About Market Risk***

Our earnings and cash flows are subject to fluctuations due to changes in interest rates primarily from our investment of available cash balances in investment grade corporate and U.S. government securities. We do not believe we are materially exposed to changes in interest rates. Under our current policies we do not use interest rate derivative instruments to manage exposure to interest rate changes. We estimated that a one percent change in interest rates would result in an approximately $1.4 million change in the fair market value of our investment portfolio at both December 31, 2004 and 2003.

Item 8. ***Financial Statements and Supplementary Data***

The financial statements required by this Item are included on pages F-1 through F-35 of this report. The supplementary financial information required by this Item is included at page F-35 of this report.

Item 9. ***Changes in and Disagreements with Accountants on Accounting and Financial Disclosure***

Not applicable.

Item 9A. ***Controls and Procedures***

Evaluation of Disclosure Controls and Procedures

The Company's management, with the participation of our chief executive officer and chief financial officer, conducted an evaluation of the effectiveness of the Company's disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934 (the "Exchange Act")), as of the end of the period covered by this Annual Report on Form 10-K. Based on this

evaluation, our chief executive officer and chief financial officer each concluded that, as of the end of such period, our disclosure controls and procedures were effective in ensuring that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized, and reported on a timely basis, and is accumulated and communicated to the Company's management, including the Company's chief executive officer and chief financial officer, as appropriate to allow timely decisions regarding required disclosure.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our management conducted an evaluation of the effectiveness of our internal control over financial reporting using the framework in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on that evaluation, our management has concluded that our internal control over financial reporting was effective as of December 31, 2004. PricewaterhouseCoopers LLP, our independent registered public accounting firm, has issued a report on management's assessment and the effectiveness of our internal control over financial reporting as of December 31, 2004, which report is included herein at page F-2.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Changes in Internal Control over Financial Reporting

There has been no change in our internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2004 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. ***Other Information***

None

PART III

Item 10. ***Directors and Officers of the Registrant***

The information required by this item (other than the information set forth in the next paragraph in this Item 10) will be included under the captions "Election of Directors," "Board Committees and Meetings," "Executive Officers of the Company," and "Section 16(a) Beneficial Ownership Reporting Compliance," in our definitive proxy statement with respect to our 2005 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

We have adopted a code of business conduct and ethics that applies to our officers, directors and employees. The full text of our code of business conduct and ethics can be found on the Company's website *(http://www.regn.com)* under the Investor Relations heading.

Item 11. ***Executive Compensation***

The information called for by this item will be included under the captions "Executive Compensation" and "Compensation of Directors" in our definitive proxy statement with respect to our 2005 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

Item 12. ***Security Ownership of Certain Beneficial Owners and Management***

The information called for by this item will be included under the captions "Security Ownership of Management," "Stock Ownership of Certain Beneficial Owners", and "Executive Compensation — Equity Compensation Plan Information", in our definitive proxy statement with respect to our 2005 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

Item 13. ***Certain Relationships and Related Transactions***

The information called for by this item will be included under the caption "Certain Relationships and Related Transactions" in our definitive proxy statement with respect to our 2005 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

Item 14. ***Principal Accountant Fees and Services***

The information called for by this item will be included under the caption "Information about Fees Paid to Independent Registered Public Accounting Firm" in our definitive proxy statement with respect to our 2005 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

(a) 1. Financial Statements

The financials statements filed as part of this report are listed on the Index to Financial Statements on page F-1.

2. Financial Statement Schedules

All schedules for which provision is made in the applicable accounting regulations of the Securities and Exchange Commission are not required under the related instructions or are inapplicable and therefore have been omitted.

3. Exhibits

Exhibit Number			Description
3.1	(a)	—	Restated Certificate of Incorporation of Regeneron Pharmaceuticals, Inc. as of June 21, 1991.
3.1.1	(b)	—	Certificate of Amendment of the Restated Certificate of Incorporation of Regeneron Pharmaceuticals, Inc., as of October 18, 1996.
3.1.2	(c)	—	Certificate of Amendment of the Certificate of Incorporation of Regeneron Pharmaceuticals, Inc., as of December 17, 2001.
3.2		—	By-Laws of the Company, currently in effect (amended through November 12, 2004).
10.1	(d)	—	1990 Amended and Restated Long-Term Incentive Plan.
10.2	(e)	—	2000 Long-Term Incentive Plan.
10.3.1	(f)	—	Amendment No. 1 to 2000 Long-Term Incentive Plan, effective as of June 14, 2002.
10.3.2	(f)	—	Amendment No. 2 to 2000 Long-Term Incentive Plan, effective as of December 20, 2002.
10.3.3	(g)	—	Amendment No. 3 to 2000 Long-term Incentive Plan, effective as of June 14, 2004.
10.3.4	(h)	—	Amendment No. 4 to 2000 Long-term Incentive Plan, effective as of November 15, 2004.
10.3.5	(i)	—	Form of option agreement and related notice of grant for use in connection with the grant of options to the Registrant's non-employee directors and named executive officers.
10.3.6	(i)	—	Form of option agreement and related notice of grant for use in connection with the grant of options to the Registrant's executive officers other than the named executive officers.

Exhibit Number			Description
10.3.7	(i)	—	Form of restricted stock award agreement and related notice of grant for use in connection with the grant of restricted stock awards to the Registrant's executive officers.
10.4	(j)*	—	Manufacturing Agreement dated as of September 18, 1995, between the Company and Merck & Co., Inc.
10.4.1*		—	Amendment No. 1 to the Manufacturing Agreement between the Company and Merck & Co., Inc., effective as of September 18, 1995.
10.4.2*		—	Amendment No. 2 to the Manufacturing Agreement between the Company and Merck & Co. Inc,, effective as of October 24, 1996.
10.4.3*		—	Amendment No. 3 to the Manufacturing Agreement between the Company and Merck & Co., Inc., effective as of December 9, 1999.
10.4.4*		—	Amendment No. 4 to the Manufacturing Agreement between the Company and Merck & Co., Inc., effective as of July 18, 2002.
10.4.5*		—	Amendment No. 5 to the Manufacturing Agreement between the Company and Merck & Co., Inc., effective as of January 1, 2005.
10.5	(k)	—	Rights Agreement, dated as of September 20, 1996, between Regeneron Pharmaceuticals, Inc. and Chase Mellon Shareholder Services LLC, as Rights Agent, including the form of Rights Certificate as Exhibit B thereto.
10.6	(f)	—	Employment Agreement, dated as of December 20, 2002, between the Company and Leonard S. Schleifer, M.D., Ph.D.
10.7*		—	Employment Agreement, dated as of December 31, 1998, between the Company and P. Roy Vagelos, M.D.
10.8	(l)	—	Indenture, dated as of October 17, 2001, between Regeneron Pharmaceuticals, Inc. and American Stock Transfer & Trust Company, as trustee.
10.9	(l)	—	Registration Rights Agreement, dated as of October 17, 2001, among Regeneron Pharmaceuticals, Inc., Merrill Lynch & Co., Merrill Lynch, Pierce, Fenner & Smith Incorporated, and Robertson Stephens, Inc.
10.10	(m)*	—	Focused Collaboration Agreement, dated as of December 31, 2000, by and between the Company and The Procter & Gamble Company.
10.11	(m)*	—	IL-1 License Agreement, dated June 26, 2002, by and among the Company, Immunex Corporation, and Amgen Inc.
10.12	(n)*	—	Collaboration, License and Option Agreement, dated as of March 28, 2003, by and between Novartis Pharma AG, Novartis Pharmaceuticals Corporation, and the Company.
10.13	(n)*	—	Stock Purchase Agreement, dates as of March 28, 2003, by and between Novartis Pharma AG and the Company.
10.14	(n)	—	Registration Rights Agreement, dates as of March 28, 2003, by and between Novartis Pharma AG and the Company.
10.15	(o)*	—	Collaboration Agreement, dates as of September 5, 2003, by and between Aventis Pharmaceuticals Inc. and Regeneron Pharmaceuticals, Inc.
10.15.1*		—	Amendment No. 1 to Collaboration Agreement, by and between Aventis Pharmaceuticals, Inc. and Regeneron Pharmaceuticals, Inc., effective as of December 31, 2004.
10.15.2	(p)		Amendment No. 2 to Collaboration Agreement, by and between Aventis Pharmaceuticals, Inc. and Regeneron Pharmaceuticals, Inc., effective as of January 7, 2005.
10.16	(o)	—	Stock Purchase Agreement, dates as of September 5, 2003, by and between Aventis Pharmaceuticals Inc. and Regeneron Pharmaceuticals, Inc.
10.17	(o)*	—	Non-Exclusive Patent License Agreement, effective as of August 18, 2003, by and between Merck & Co., Inc. and Regeneron Pharmaceuticals, Inc.
12.1		—	Statement re: computation of ratio of earnings to combined fixed charges of Regeneron Pharmaceuticals, Inc.

Exhibit Number			Description
18.1	(o)	—	Independent Accountant's Preferability Letter Regarding a Change in Accounting Principle.
23.1		—	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.
31.1		—	Certification of CEO pursuant to Rule 13a-14(a) under the Securities and Exchange Act of 1934.
31.2		—	Certification of CFO pursuant to Rule 13a-14(a) under the Securities and Exchange Act of 1934.
32		—	Certification of CEO and CFO pursuant to 18 U.S.C. Section 1350.

Description:

(a) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended June 30, 1991, filed August 13, 1991.

(b) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended September 30, 1996, filed November 5, 1996.

(c) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc. for the fiscal year ended December 31, 2001, filed March 22, 2002.

(d) Incorporated by reference from the Company's registration statement on Form S-1 (file number 33-39043).

(e) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc. for the quarter ended December 31, 2001, filed March 22, 2002.

(f) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc. for the fiscal year ended December 31, 2002, filed March 31, 2003.

(g) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended June 30, 2004, filed August 5, 2004.

(h) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc. filed November 17, 2004.

(i) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc. filed December 13, 2004.

(j) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended September 30, 1995, filed November 14, 1995.

(k) Incorporated by reference from the Form 8-A for Regeneron Pharmaceuticals, Inc. filed October 15, 1996.

(l) Incorporated by reference from the Company's registration statement on Form S-3 (file number 333-74464).

(m) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended June 30, 2002, filed August 13, 2002.

(n) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended March 31, 2003, filed May 15, 2003.

(o) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc. for the quarter ended September 30, 2003, filed November 11, 2003.

(p) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc. filed January 11, 2005.

* Portions of this document have been omitted and filed separately with the Commission pursuant to requests for confidential treatment pursuant to Rule 24b-2.

SIGNATURE

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Regeneron Pharmaceuticals, Inc.

By: /s/ Leonard S. Schleifer

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

Dated: New York, New York
March 11, 2005

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Leonard S. Schleifer, President and Chief Executive Officer, and Murray A. Goldberg, Senior Vice President, Finance & Administration, Chief Financial Officer, Treasurer, and Assistant Secretary, and each of them, his true and lawful attorney-in-fact and agent, with the full power of substitution and resubstitution, for him and in his name, place, and stead, in any and all capacities therewith, to sign any and all amendments to this report on Form 10-K, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto each said attorney-in-fact and agent full power and authority to do and perform each and every act in person, hereby ratifying and confirming all that each said attorney-in-fact and agent, or either of them, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated:

Signature	Title
/s/ Leonard S. Shleifer Leonard S. Schleifer, M.D., Ph.D.	President, Chief Executive Officer, and Director (Principal Executive Officer)
/s/ Murray A. Goldberg Murray A. Goldberg	Senior Vice President, Finance & Administration, Chief Financial Officer, Treasurer, and Assistant Secretary (Principal Financial Officer)
/s/ Douglas S. McCorkle Douglas S. McCorkle	Controller and Assistant Treasurer (Principal Accounting Officer)
/s/ George D. Yancopoulos George D. Yancopoulos, M.D., Ph.D	Executive Vice President, Chief Scientific Officer, President, Regeneron Research Laboratories, and Director
/s/ P. Roy Vagelos P. Roy Vagelos, M.D.	Chairman of the Board
/s/ Charles A. Baker Charles A. Baker	Director
/s/ Michael S. Brown Michael S. Brown, M.D.	Director

Signature	Title
/s/ Alfred G. Gilman Alfred G. Gilman, M.D., Ph.D.	Director
/s/ Joseph L. Goldstein Joseph L. Goldstein, M.D.	Director
/s/ Arthur F. Ryan Arthur F. Ryan	Director
/s/ Eric M. Shooter Eric M. Shooter, Ph.D.	Director
/s/ George L. Sing George L. Sing	Director

REGENERON PHARMACEUTICALS, INC.

INDEX TO FINANCIAL STATEMENTS

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of
Regeneron Pharmaceuticals, Inc.:

We have completed an integrated audit of Regeneron Pharmaceutical Inc.'s 2004 financial statements and of its internal control over financial reporting as of December 31, 2004 and audits of its 2003 and 2002 financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Our opinions, based on our audits, are presented below.

Financial statements

In our opinion, the financial statements listed in the accompanying index present fairly, in all material respects, the financial position of Regeneron Pharmaceuticals, Inc. at December 31, 2004 and 2003, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2004 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit of financial statements includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

Internal control over financial reporting

Also, in our opinion, management's assessment, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A, that the Company maintained effective internal control over financial reporting as of December 31, 2004 based on criteria established in *Internal Control — Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO), is fairly stated, in all material respects, based on those criteria. Furthermore, in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004 based on criteria established in *Internal Control — Integrated Framework* issued by the COSO. The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express opinions on management's assessment and on the effectiveness of the Company's internal control over financial reporting based on our audit. We conducted our audit of internal control over financial reporting in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. An audit of internal control over financial reporting includes obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we consider necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinions.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (i) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (ii) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the

company; and (iii) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

PricewaterhouseCoopers LLP

New York, New York
March 7, 2005

REGENERON PHARMACEUTICALS, INC.

BALANCE SHEETS
December 31, 2004 and 2003

	2004	2003
	(In thousands, except share data)	
ASSETS		
Current assets		
Cash and cash equivalents	$ 101,234	$ 118,285
Marketable securities	194,748	164,576
Restricted marketable securities		10,913
Accounts receivable	43,102	15,529
Prepaid expenses and other current assets	1,642	1,898
Inventory	3,229	9,006
Total current assets	343,955	320,207
Marketable securities	52,930	72,792
Property, plant, and equipment, at cost, net of accumulated depreciation and amortization	71,239	80,723
Other assets	4,984	5,833
Total assets	$ 473,108	$ 479,555
LIABILITIES and STOCKHOLDERS' EQUITY		
Current liabilities		
Accounts payable and accrued expenses	$ 18,872	$ 18,933
Deferred revenue, current portion	15,267	40,173
Loan payable to Novartis Pharma AG		13,817
Total current liabilities	34,139	72,923
Deferred revenue	56,426	68,830
Notes payable	200,000	200,000
Other long-term liabilities		159
Total liabilities	290,565	341,912
Commitments and contingencies		
Stockholders' equity		
Preferred stock, $.01 par value; 30,000,000 shares authorized; issued and outstanding — none		
Class A Stock, convertible, $.001 par value; 40,000,000 shares authorized; 2,358,373 shares issued and outstanding in 2004 2,365,873 shares issued and outstanding in 2003	2	2
Common Stock, $.001 par value; 160,000,000 shares authorized; 53,502,004 shares issued and outstanding in 2004 53,165,635 shares issued and outstanding in 2003	54	53
Additional paid-in capital	675,389	673,118
Unearned compensation	(2,299)	(4,101)
Accumulated deficit	(489,834)	(531,533)
Accumulated other comprehensive (loss) income	(769)	104
Total stockholders' equity	182,543	137,643
Total liabilities and stockholders' equity	$ 473,108	$ 479,555

The accompanying notes are an integral part of the financial statements.

REGENERON PHARMACEUTICALS, INC.

STATEMENTS OF OPERATIONS
for the Years Ended December 31, 2004, 2003, and 2002

	2004	2003	2002
	(In thousands, except per share data)		
Revenues			
Contract research and development	$ 113,157	$ 47,366	$ 10,924
Research progress payments	42,770		
Contract manufacturing	18,090	10,131	11,064
	174,017	57,497	21,988
Expenses			
Research and development	136,095	136,024	124,953
Contract manufacturing	15,214	6,676	6,483
General and administrative	17,062	14,785	12,532
	168,371	157,485	143,968
Income (loss) from operations	5,646	(99,988)	(121,980)
Other income (expense)			
Other contract income	42,750		
Investment income	5,478	4,462	9,462
Interest expense	(12,175)	(11,932)	(11,859)
	36,053	(7,470)	(2,397)
Net income (loss)	$ 41,699	$ (107,458)	$ (124,377)
Net income (loss) per share:			
Basic	$ 0.75	$ (2.13)	$ (2.83)
Diluted	$ 0.74	$ (2.13)	$ (2.83)

The accompanying notes are an integral part of the financial statements.

REGENERON PHARMACEUTICALS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY
For the Years Ended December 31, 2004, 2003, and 2002

	Class A Stock		Common Stock		Additional Paid-In	Unearned	Accumulated	Accumulated Other Comprehensive	Total Stockholders'	Comprehensive
	Shares	Amount	Shares	Amount	Capital	Compensation	Deficit	Income (Loss)	Equity	Loss
						(In thousands)				
Balance, December 31, 2001	2,563	$ 3	41,264	$ 41	$ 567,624	$ (2,789)	$ (299,698)	$ 1,174	$ 266,355	
Issuance of Common Stock in connection with exercise of stock options, net of shares tendered			251		2,149				2,149	
Issuance of Common Stock in connection with Company 401(k) Savings Plan contribution			22		764				764	
Conversion of Class A Stock to Common Stock	(72)	(1)	72	1						
Issuance of restricted Common Stock under Long-Term Incentive Plan, net of forfeitures			137		2,644	(2,644)				
Amortization of unearned compensation						1,790			1,790	
Issuance of stock options in consideration for consulting services					3				3	
Net loss, 2002							(124,377)		(124,377)	$ (124,377)
Change in net unrealized gain (loss) on marketable securities								(703)	(703)	(703)
Balance, December 31, 2002	2,491	2	41,746	42	573,184	(3,643)	(424,075)	471	145,981	$ (125,080)
Issuance of Common Stock in connection with exercise of stock options, net of shares tendered			601		1,941				1,941	
Issuance of Common Stock to Novartis Pharma AG			7,527	8	47,992				48,000	
Issuance of Common Stock to the sanofi-aventis Group			2,800	3	44,997				45,000	
Issuance of Common Stock to Merck & Co. Inc.			109		1,500				1,500	
Issuance of Common Stock in connection with Company 401(k) Savings Plan contribution			43		747				747	
Conversion of Class A Stock to Common Stock	(125)		125							
Issuance of restricted Common Stock under Long-Term Incentive Plan, net of forfeitures			215		2,757	(2,757)				
Amortization of unearned compensation						2,299			2,299	
Net loss, 2003							(107,458)		(107,458)	$ (107,458)
Change in net unrealized gain (loss) on marketable securities								(367)	(367)	(367)
Balance, December 31, 2003	2,366	2	53,166	53	673,118	(4,101)	(531,533)	104	137,643	$ (107,825)

(Continued)

REGENERON PHARMACEUTICALS, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY — (Continued)
For the Years Ended December 31, 2004, 2003, and 2002

	Class A Stock		Common Stock		Additional Paid-in Capital	Unearned Compensation	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Total Stockholders' Equity	Comprehensive Loss
	Shares	Amount	Shares	Amount						
	(In thousands, except per share data)									
Issuance of Common Stock in connection with exercise of stock options, net of shares tendered			286	1	1,501				1,502	
Repurchase of Common Stock from Merck & Co., Inc.			(109)		(888)				(888)	
Issuance of Common Stock in connection with Company 401(k) Savings Plan contribution			64		917				917	
Conversion of Class A Stock to Common Stock	(8)		8							
Issuance of restricted Common Stock under Long-Term Incentive Plan, net of forfeitures			87		741	(741)				
Amortization of unearned compensation						2,543			2,543	
Net income, 2004							41,699		41,699	$ 41,699
Change in net unrealized gain (loss) on marketable securities								(873)	(873)	(873)
Balance, December 31, 2004	2,358	$ 2	53,502	$ 54	$ 675,389	$ (2,299)	$ (489,834)	$ (769)	$ 182,543	$ 40,826

The accompanying notes are an integral part of the financial statements.

REGENERON PHARMACEUTICALS, INC.

STATEMENTS OF CASH FLOWS
For the Years Ended December 31, 2004, 2003, and 2002

	2004	2003	2002
		(In thousands)	
Cash flows from operating activities			
Net income (loss)	$ 41,699	$ (107,458)	$ (124,377)
Adjustments to reconcile net income (loss) to net cash used in operating activities			
Depreciation and amortization	15,362	12,937	8,454
Non-cash compensation expense	2,543	2,562	1,793
Non-cash expense related to a license agreement		1,500	
Forgiveness of loan payable to Novartis Pharma AG, inclusive of accrued interest	(17,770)		
Changes in assets and liabilities			
Increase in accounts receivable	(27,573)	(11,512)	(1,042)
(Increase) decrease in prepaid expenses and other assets	(1,799)	589	184
Decrease (increase) in inventory	6,914	(1,049)	(1,732)
(Decrease) increase in deferred revenue	(37,310)	93,869	1,498
Increase in accounts payable, accrued expenses, and other liabilities	1,025	2,429	4,699
Total adjustments	(58,608)	101,325	13,854
Net cash used in operating activities	(16,909)	(6,133)	(110,523)
Cash flows from investing activities			
Purchases of marketable securities	(265,243)	(276,447)	(234,463)
Purchases of restricted marketable securities	(11,075)	(11,055)	(5,514)
Sales or maturities of marketable securities	255,783	231,261	199,317
Maturities of restricted marketable securities	22,126	22,054	16,514
Capital expenditures	(6,174)	(29,656)	(34,370)
Net cash used in investing activities	(4,583)	(63,843)	(58,516)
Cash flows from financing activities			
Net proceeds from issuances of Common Stock	1,502	94,678	2,149
Repurchase of Common Stock	(888)		
Borrowings under loan payable	3,827	13,656	
Capital lease payments		(150)	(426)
Net cash provided by financing activities	4,441	108,184	1,723
Net (decrease) increase in cash and cash equivalents	(17,051)	38,208	(167,316)
Cash and cash equivalents at beginning of period	118,285	80,077	247,393
Cash and cash equivalents at end of period	$ 101,234	$ 118,285	$ 80,077
Supplemental disclosure of cash flow information			
Cash paid for interest	$ 11,007	$ 11,003	$ 11,038

The accompanying notes are an integral part of the financial statements.

REGENERON PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS

For the years ended December 31, 2004, 2003, and 2002

(Unless otherwise noted, dollars in thousands, except per share data)

1. Organization and Business

Regeneron Pharmaceuticals, Inc. (the "Company" or "Regeneron") was incorporated in January 1988 in the State of New York. The Company is engaged in research and development programs to discover and commercialize therapeutics to treat human disorders and conditions. The Company's facilities are located in New York. The Company's business is subject to certain risks including, but not limited to, uncertainties relating to conducting pharmaceutical research, obtaining regulatory approvals, commercializing products, and obtaining and enforcing patents.

2. Summary of Significant Accounting Policies

Property, Plant, and Equipment

Property, plant, and equipment are stated at cost. Depreciation is provided on a straight-line basis over the estimated useful lives of the assets. Expenditures for maintenance and repairs which do not materially extend the useful lives of the assets are charged to expense as incurred. The cost and accumulated depreciation or amortization of assets retired or sold are removed from the respective accounts, and any gain or loss is recognized in operations. The estimated useful lives of property, plant, and equipment are as follows:

Building and improvements	6-30 years
Leasehold improvements	Life of lease
Laboratory and computer equipment	3-5 years
Furniture and fixtures	5 years

Costs of construction of certain long-lived assets include capitalized interest which is amortized over the estimated useful life of the related asset. The Company capitalized interest costs of $0.3 million and $0.2 million in 2003 and 2002, respectively. The Company did not capitalize any interest costs in 2004.

The Company periodically assesses the recoverability of property and equipment and evaluates such assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Asset impairment is determined to exist if estimated future undiscounted cash flows are less than the carrying amount in accordance with Statement of Financial Accounting Standards No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*. As of December 31, 2004, there were no impairments of long-lived assets.

Cash and Cash Equivalents

For purposes of the statement of cash flows and the balance sheet, the Company considers all highly liquid debt instruments with a maturity of three months or less when purchased to be cash equivalents. The carrying amount reported in the balance sheet for cash and cash equivalents approximates its fair value.

Inventories

Inventories are stated at the lower of cost or market. Cost is determined based on standards that approximate the first-in, first-out method. Inventories are shown net of applicable reserves.

Revenue Recognition and Change in Accounting Principle

a. Contract Research and Development and Research Progress Payments

The Company recognizes revenue from contract research and development and research progress payments in accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition* ("SAB 104") and

FASB Emerging Issue Task Force Issue No. 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables* ("EITF 00-21"). SAB 104 superseded Staff Accounting Bulletin No. 101, *Revenue Recognition in Financial Statement* ("SAB 101"), in December 2003. During the third quarter of 2003, the Company elected to change the method it uses to recognize revenue under SAB 101 related to non-refundable collaborator payments, including up-front licensing payments, payments for development activities, and research progress (milestone) payments, to the Substantive Milestone Method, adopted retroactively to January 1, 2003. There was no cumulative effect of this change in accounting principle on prior periods. Under this method, the Company recognizes revenue from non-refundable up-front license payments, not tied to achieving a specific performance milestone, ratably over the period over which the Company expects to perform services. Payments for development activities are recognized as revenue as earned, ratably over the period of effort. Substantive at-risk milestone payments, which are based on achieving a specific performance milestone, are recognized as revenue when the milestone is achieved and the related payment is due, provided there is no future service obligation associated with that milestone. The change in accounting method was made because the Company believes that it better reflects the substance of the Company's collaborative agreements and is more consistent with current practices in the biotechnology industry.

Previously, the Company had recognized revenue from non-refundable collaborator payments based on the percentage of costs incurred to date, estimated costs to complete, and total expected contract revenue. However, the revenue recognized was limited to the amount of non-refundable payments received. This accounting method was adopted on January 1, 2000 upon the release of SAB 101. The cumulative effect of adopting SAB 101 at January 1, 2000 amounted to $1.6 million of additional loss, with a corresponding increase to deferred revenue that has been recognized in subsequent periods, of which $0.1 million, $0.4 million, and $0.4 million, respectively, was included in contract research and development revenue in 2004, 2003, and 2002. The $1.6 million represented a portion of a 1989 payment received from Sumitomo Chemical Co. Ltd. in consideration for a fifteen year limited right of first negotiation to license up to three of the Company's product candidates in Japan (see Note 11d). The effect of income taxes on the cumulative effect adjustment was immaterial.

b. Contract Manufacturing

The Company has entered into a contract manufacturing agreement under which it manufactures product and performs services for a third party. Contract manufacturing revenue is recognized as product is shipped and as services are performed (see Note 12).

Investment Income

Interest income, which is included in investment income, is recognized as earned.

Accounting for the Impairment of Long-Lived Assets

Long-lived assets, such as fixed assets, are reviewed for impairment when events or circumstances indicate that their carrying value may not be recoverable. Estimated undiscounted expected future cash flows are used to determine if an asset is impaired in which case the asset's carrying value would be reduced to fair value. For all periods presented, no impairment losses were recorded.

Patents

As a result of the Company's research and development efforts, it has obtained, applied for, or is applying for a number of patents to protect proprietary technology and inventions. All costs associated with patents are expensed as incurred.

Research and Development Expenses

Research and development expenses include costs directly attributable to the conduct of research and development programs, including the cost of salaries, payroll taxes, employee benefits, materials, supplies, depreciation on and maintenance of research equipment, costs related to research collaboration and licensing agreements (see Note 10e), the cost of services provided by outside contractors, including services related to the Company's clinical trials, clinical trial expenses, the full cost of manufacturing drug for use in research, preclinical development, and clinical trials, expenses related to the development of manufacturing processes prior to commencing commercial production of a product under contract manufacturing arrangements, and the allocable portions of facility costs, such as rent, utilities, insurance, repairs and maintenance, depreciation, and general support services. All costs associated with research and development are expensed as incurred.

For each clinical trial that the Company conducts, certain clinical trial costs, which are included in research and development expenses, are expensed based on the expected total number of patients in the trial, the rate at which patients enter the trial, and the period over which clinical investigators or contract research organizations are expected to provide services. During the course of a clinical trial, the Company adjusts its rate of clinical expense recognition if actual results differ from the Company's estimates.

Per Share Data

Net income (loss) per share, basic and diluted, is computed on the basis of the net income (loss) for the period divided by the weighted average number of shares of Common Stock and Class A Stock outstanding during the period. The basic net income (loss) per share excludes restricted stock awards until vested. The diluted net income per share for the year ended December 31, 2004 is based upon the weighted average number of shares of Common Stock and Class A Stock and the common stock equivalents outstanding when dilutive. Common stock equivalents include: (i) outstanding stock options and restricted stock awards under the Company's Long-Term Incentive Plans, which are included under the treasury stock method when dilutive, and (ii) Common Stock to be issued under the assumed conversion of the Company's outstanding convertible senior subordinated notes, which are included under the if-converted method when dilutive. The computation of diluted net loss per share for the years ended December 31, 2003 and 2002 does not include common stock equivalents, since such inclusion would be antidilutive. Disclosures required by Statement of Financial Accounting Standards No. 128, *Earnings per Share,* have been included in Note 17.

Income Taxes

The Company recognizes deferred tax liabilities and assets for the expected future tax consequences of events that have been included in the financial statements or tax returns. Under this method, deferred tax liabilities and assets are determined on the basis of the difference between the tax basis of assets and liabilities and their respective financial reporting amounts ("temporary differences") at enacted tax rates in effect for the years in which the differences are expected to reverse. A valuation allowance is established for deferred tax assets for which realization is uncertain. See Note 15.

Comprehensive Income (Loss)

Comprehensive income (loss) represents the change in net assets of a business enterprise during a period from transactions and other events and circumstances from non-owner sources. Comprehensive income (loss) of the Company includes net income (loss) adjusted for the change in net unrealized gain or loss on marketable securities. The net effect of income taxes on comprehensive income (loss) is immaterial. Comprehensive income for the year ended December 31, 2004 and comprehensive losses for the years ended December 31, 2003 and 2002 have been included in the Statements of Stockholders' Equity.

Concentrations of Credit Risk

Financial instruments which potentially subject the Company to concentrations of credit risk consist of cash, cash equivalents, marketable securities, restricted marketable securities, and receivables from the sanofi-aventis Group, The Procter & Gamble Company, and Merck & Co., Inc. The Company generally invests its excess cash in obligations of the U.S. government and its agencies, bank deposits, investment grade debt securities issued by corporations, governments, and financial institutions, and money market funds that invest in these instruments. The Company has established guidelines that relate to credit quality, diversification, and maturity, and that limit exposure to any one issue of securities.

Risks and Uncertainties

Regeneron has had no sales of its products and there is no assurance that the Company's research and development efforts will be successful, that the Company will ever have commercially approved products, or that the Company will achieve significant sales of any such products. The Company has generally incurred net losses and negative cash flows from operations since its inception, and revenues to date have principally been limited to payments for research from our collaborators and for contract manufacturing from two pharmaceutical companies and investment income. The Company operates in an environment of rapid change in technology and is dependent upon the services of its employees, consultants, collaborators, and certain third-party suppliers, including single-source unaffiliated third-party suppliers of certain raw materials and equipment. Regeneron, as licensee, licenses certain technologies that are important to the Company's business which impose various obligations on the Company. If Regeneron fails to comply with these requirements, licensors may have the right to terminate the Company's licenses.

Contract research and development revenue in 2004 was primarily earned from the sanofi-aventis Group, Novartis Pharma AG, and The Procter & Gamble Company under collaboration agreements (see Notes 11a, 11b and 11e). Under the collaboration agreement with sanofi-aventis, agreed upon VEGF Trap development expenses incurred by Regeneron during the term of the agreement will be funded by sanofi-aventis. In addition, the Company earned a $25.0 million payment in 2004 upon achievement of an early-stage clinical milestone and may receive up to $360.0 million in additional milestone payments upon receipt of specified VEGF Trap marketing approvals. Sanofi-aventis has the right to terminate the agreement without cause with at least twelve months advance notice. Under the collaboration agreement with Novartis, agreed upon IL-1 Trap development expenses were shared equally by the Company and Novartis in 2003. In February 2004, Novartis provided notice of its intention not to proceed with the joint development of the IL-1 Trap and the Company subsequently recognized contract research and development revenue equal to the remaining balance of a 2003 up-front payment from Novartis that had been deferred. Under the long-term collaboration with Procter & Gamble, Procter & Gamble is obligated to provide payments to fund Regeneron research of $2.5 million per quarter, before adjustments for inflation, through December 2005, with no further research obligations by either party thereafter. Contract manufacturing revenue in 2004 was earned from Merck & Co., Inc. under a long-term manufacturing agreement that extends, as amended, through October 2006 (see Note 12), but may be terminated at any time by Merck upon Merck's payment of a termination fee and may be extended by Merck, upon twelve-months' prior notice, for an additional year through October 2007.

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates. Significant estimates include useful lives of property, plant, and equipment, the periods over which certain revenues and expenses will be recognized including contract research and development revenue recognized from non-refundable up-front licensing payments, contract manufacturing revenue recognized from reimbursed, deferred capital costs,

(Unless otherwise noted, dollars in thousands, except per share data)

and expense recognition of certain clinical trial costs which are included in research and development expenses, and the extent to which deferred tax assets and liabilities are offset by a valuation allowance.

Stock-based Employee Compensation

The accompanying financial position and results of operations of the Company have been prepared in accordance with APB Opinion No. 25, *Accounting for Stock Issued to Employees* ("APB No. 25"). Under APB No. 25, generally, no compensation expense is recognized in the accompanying financial statements in connection with the awarding of stock option grants to employees provided that, as of the grant date, all terms associated with the award are fixed and the quoted market price of the Company's stock, as of the grant date, is equal to or less than the amount an employee must pay to acquire the stock as defined.

The Company has stock-based incentive plans, which are more fully described in Note 13a. The following table illustrates the effect on the Company's net income (loss) and net income (loss) per share had compensation costs for the incentive plans been determined in accordance with the fair value based method of accounting for stock-based compensation as prescribed by Statement of Financial Accounting Standards No. 123, *Accounting for Stock-Based Compensation* ("SFAS No. 123"). Since option grants awarded during 2004, 2003, and 2002 vest over several years and additional awards are expected to be issued in the future, the pro forma results shown below are not likely to be representative of the effects on future years of the application of the fair value based method.

	2004	2003	2002
Net income (loss), as reported	$ 41,699	$ (107,458)	$ (124,377)
Add: Stock-based employee compensation expense included in reported net income (loss)	2,543	2,562	1,790
Deduct: Total stock-based employee compensation expense determined under fair value based method for all awards	(36,093)	(45,048)	(45,676)
Pro forma net income (loss), basic	$ 8,149	$ (149,944)	$ (168,263)
Basic net income (loss) per share amounts:			
As reported	$ 0.75	$ (2.13)	$ (2.83)
Pro forma	$ 0.15	$ (2.97)	$ (3.83)
Diluted net income (loss) per share amounts:			
As reported	$ 0.74	$ (2.13)	$ (2.83)
Pro forma	$ 0.15	$ (2.97)	$ (3.83)

In 2003, the Company's Chief Executive Officer was granted permission by the Board of Directors to initiate a one-time net cashless exercise of stock options. Upon completion of the net cashless exercise, the Company recognized $0.3 million of compensation expense, which equaled the excess of the fair market value of the shares over the option exercise price on the date that the Board of Directors granted its consent for the transaction.

Effective January 1, 2005, the Company intends to adopt the fair value based method of accounting for stock-based employee compensation under the provisions of SFAS No. 123, as modified by Statement of Financial Accounting Standards No. 148, *Accounting for Stock Based Compensation — Transition and Disclosure* ("SFAS No. 148"), using the modified prospective method. SFAS Nos. 123/148 require that compensation expense in an amount equal to the fair market value of the share-based payment (including stock option awards) be recognized over the vesting period of the awards. Under the modified prospective method, compensation cost will be recognized beginning January 1, 2005 for (a) all share based payments

granted on or after January 1, 2005, including replacement options granted under the Company's stock option exchange program (see Note 13a) and (b) all awards granted to employees prior to January 1, 2005 that remain unvested on that date. The Company will recognize this compensation cost in each of the categories of expense in the Company's Statement of Operations.

Other disclosures required by SFAS No. 123 have been included in Note 13a.

Statement of Cash Flows

Supplemental disclosure of noncash investing and financing activities:

In 2004, 2003, and 2002, the Company awarded 105,052, 219,367, and 139,611 shares, respectively, of Restricted Stock under the Regeneron Pharmaceuticals, Inc. Long-Term Incentive Plan (see Note 13a). The Company records unearned compensation in Stockholders' Equity related to these awards based on the fair market value of shares of the Company's Common Stock on the grant date of the Restricted Stock award, which is expensed, on a pro rata basis, over the period that the restrictions on these shares lapse. In 2004, 2003, and 2002, the Company recognized $2.5 million, $2.3 million, and $1.8 million, respectively, of compensation expense related to Restricted Stock awards.

Included in accounts payable and accrued expenses at December 31, 2004, 2003, and 2002 were $0.6 million, $0.8 million, and $13.5 million of capital expenditures, respectively.

Included in accounts payable and accrued expenses at December 31, 2003, 2002, and 2001 were $0.9 million, $0.7 million, and $0.8 million, respectively, of accrued 401(k) Savings Plan contribution expense. During the first quarter of 2004, 2003, and 2002, the Company contributed 64,333, 42,543, and 21,953 shares, respectively, of Common Stock to the 401(k) Savings Plan in satisfaction of these obligations.

Included in marketable securities at December 31, 2004, 2003, and 2002 were $2.6 million, $0.9 million, and $2.0 million of accrued interest income, respectively.

Future Impact of Recently Issued Accounting Standards

In April 2004, the Emerging Issues Task Force issued Statement No. 03-6, *Participating Securities and the Two — Class Method under FASB Statement No. 128, Earnings per Share* ("EITF 03-6"). EITF 03-6 addresses a number of questions regarding the computation of earnings per share ("EPS") by companies that have issued securities other than common stock that contractually entitle the holder to participate in dividends and earnings of the company when, and if, it declares dividends on its common stock. EITF 03-6 defines participation rights based solely on whether the holder would be entitled to receive any dividends if the entity declared them during the period and requires the use of the two-class method for computing basic EPS when participating convertible securities exist. In addition, EITF 03-6 expands the use of the two-class method to encompass other forms of participating securities and is effective for fiscal periods beginning after March 31, 2004. Since the Company has no participating securities, the Company's adoption of EITF 03-6 did not have an impact on the Company's financial statements.

In November 2004, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards No. 151, *Inventory Costs, an amendment of ARB 43, Chapter 4* ("SFAS No. 151"). SFAS No. 151 clarifies the accounting for abnormal amounts of idle facility expense, freight, handling costs, and wasted material by requiring that those items be recognized as current-period charges in all circumstances. SFAS No. 151 is effective for fiscal years beginning after June 15, 2005. Management believes that the future adoption of SFAS No. 151 will not have a material impact on the Company's financial statements.

In December 2004, the FASB issued Statement of Financial Accounting Standards No. 123R, *Share-Based Payment* ("SFAS No. 123R"). SFAS No. 123R is a revision of SFAS No. 123, *Accounting for*

Stock-Based Compensation, and supersedes APB Opinion No. 25, *Accounting for Stock Issued to Employees,* and its related implementation guidance. SFAS No. 123R establishes standards for the accounting for transactions in which an entity exchanges its equity instruments for goods or services. SFAS No. 123R focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions, and requires the recognition of compensation expense in an amount equal to the fair value of the share-based payment (including stock options and restricted stock) issued to employees. SFAS No. 123R is effective for fiscal periods beginning after June 15, 2005. The Company currently intends to adopt SFAS No. 123R effective July 1, 2005 using the modified prospective method. Under the modified prospective method, compensation cost is recognized beginning with the effective date based on (a) the requirements of SFAS No. 123R for all share-based payments granted after the effective date and (b) the requirements of SFAS No. 123 for all awards granted to employees prior to the effective date of SFAS No. 123R that remain unvested on the effective date. Although the impact of adopting SFAS No. 123R has not yet been quantified, management believes that the future adoption of this standard will have a material impact on the Company's financial statements.

In December 2004, the FASB issued Statement of Financial Accounting Standards No. 153, *Exchanges of Nonmonetary Assets, an amendment of APB Opinion No. 29 ("SFAS No. 153")*. SFAS No. 153 eliminates an exception for nonmonetary exchanges of similar productive assets under APB Opinion No. 29, and replaces it with a general exception for exchanges of nonmonetary assets that do not have commercial substance. SFAS No. 153 is to be applied prospectively and is effective for nonmonetary asset exchanges occurring in fiscal periods beginning after June 15, 2005. Management believes that the future adoption of SFAS No. 153 will not have a material impact on the Company's financial statements.

3. Marketable Securities

The Company considers its unrestricted marketable securities to be "available-for-sale," as defined by Statement of Financial Accounting Standards No. 115, *Accounting for Certain Investments in Debt and Equity Securities*. Gross unrealized holding gains and losses are reported as a net amount in a separate component of stockholders' equity entitled Accumulated Other Comprehensive Income (Loss). The net change in unrealized holding gains and losses is excluded from operations and included in stockholders' equity as a separate component of comprehensive loss.

REGENERON PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS — (Continued)

(Unless otherwise noted, dollars in thousands, except per share data)

The following tables summarize the amortized cost basis of marketable securities, the aggregate fair value of marketable securities, and gross unrealized holding gains and losses at December 31, 2004 and 2003:

	Amortized Cost Basis	Fair Value	Unrealized Holding Gains	Unrealized Holding (Losses)	Unrealized Holding Net
At December 31, 2004					
Maturities within one year					
Corporate debt securities	$ 58,077	$ 57,971	$ 8	$ (114)	$ (106)
U.S. government securities	137,105	136,777	—	(328)	(328)
	195,182	194,748	8	(442)	(434)
Maturities between one and two years					
U.S. government securities	53,265	52,930	—	(335)	(335)
	$ 248,447	$ 247,678	$ 8	$ (777)	$ (769)
At December 31, 2003					
Maturities within one year					
Corporate debt securities	$ 40,586	$ 40,578	$ 6	$ (14)	$ (8)
U.S. government securities	123,893	123,998	107	(2)	105
	164,479	164,576	113	(16)	97
Maturities between one and two years					
Corporate debt securities	28,928	28,931	18	(15)	3
U.S. government securities	40,749	40,803	54		54
Asset-backed securities	3,108	3,058	—	(50)	(50)
	72,785	72,792	72	(65)	7
	$ 237,264	$ 237,368	$ 185	$ (81)	$ 104

Realized gains and losses are included as a component of investment income. For the years ended December 31, 2004, 2003, and 2002, gross realized gains and losses were not significant. In computing realized gains and losses, the Company computes the cost of its investments on a specific identification basis. Such cost includes the direct costs to acquire the securities, adjusted for the amortization of any discount or premium. The fair value of marketable securities has been estimated based on quoted market prices.

The following table shows the unrealized losses and fair value of the Company's marketable securities with unrealized losses that are not deemed to be other-than-temporarily impaired, aggregated by investment category and length of time that individual securities have been in a continuous unrealized loss position, at December 31, 2004. These securities mature at various dates through May 2006.

	Less than 12 Months		12 Months or Greater		Total	
Description of Security	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss
Corporate debt securities	$ 29,267	$ 93	$ 7,353	$ 21	$ 36,620	$ 114
U.S. government securities	189,707	663	0	0	$ 189,707	663
	$ 218,974	$ 756	$ 7,353	$ 21	$ 226,327	$ 777

The unrealized losses on the Company's investments in corporate debt securities and U.S. government securities were primarily caused by interest rate increases, which have generally resulted in a decrease in the

(Unless otherwise noted, dollars in thousands, except per share data)

market value of the Company's portfolio. Based upon the Company's currently projected sources and uses of cash, the Company intends to hold these securities until a recovery of fair value, which may be maturity. Therefore, the Company does not consider these marketable securities to be other-than-temporarily impaired at December 31, 2004. Unrealized holding losses on marketable securities at December 31, 2003 were losses for less than twelve months.

4. Accounts Receivable

Accounts receivable as of December 31, 2004 and 2003 consist of the following:

	2004	2003
Receivable from the sanofi-aventis Group (see Note 11a)	$ 39,362	$ 8,917
Receivable from Novartis Pharma AG (see Note 11b)	—	3,177
Receivable from The Procter & Gamble Company (see Note 11e)	2,345	2,670
Receivable from Merck & Co. Inc. (see Note 12)	1,315	765
Other	80	—
	$ 43,102	$ 15,529

5. Inventories

Inventory balances at December 31, 2004 and 2003 consist of raw materials, work-in process, and finished products associated with the production of an intermediate for a Merck & Co., Inc. pediatric vaccine under a long-term manufacturing agreement (see Note 12).

Inventories as of December 31, 2004 and 2003 consist of the following:

	2004	2003
Raw materials	$ 310	$ 388
Work-in process	692(1)	—(2)
Finished products	2,227	8,618
	$ 3,229	$ 9,006

(1) Net of reserves of $0.3 million.

(2) Net of reserves of $0.2 million.

REGENERON PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS — (Continued)
(Unless otherwise noted, dollars in thousands, except per share data)

6. Property, Plant, and Equipment

Property, plant, and equipment as of December 31, 2004 and 2003 consist of the following:

	2004	2003
Land	$ 475	$ 475
Building and improvements	56,750	56,054
Leasehold improvements	30,451	29,108
Construction-in-progress	172	1,443
Laboratory and other equipment	55,174	51,536
Furniture, fixtures, and computer equipment	5,498	5,092
	148,520	143,708
Less, accumulated depreciation and amortization	(77,281)	(62,985)
	$ 71,239	$ 80,723

Depreciation and amortization expense on property, plant, and equipment amounted to $14.3 million, $13.0 million, and $8.5 million, for the years ended December 31, 2004, 2003, and 2002, respectively. Included in these amounts was $1.1 million of depreciation and amortization expense related to contract manufacturing that was capitalized into inventory for each of the three years ended December 31, 2004, 2003, and 2002.

7. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses as of December 31, 2004 and 2003 consist of the following:

	2004	2003
Accounts payable	$ 4,407	$ 3,878
Accrued payroll and related costs	7,972	5,125
Accrued clinical trial expense	2,083	3,876
Accrued expenses, other	2,118	3,762
Interest payable on convertible notes	2,292	2,292
	$ 18,872	$ 18,933

REGENERON PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS — (Continued)
(Unless otherwise noted, dollars in thousands, except per share data)

8. Deferred Revenue

Deferred revenue as of December 31, 2004 and 2003 consists of the following:

	2004	2003
Current portion:		
Received from the sanofi-aventis Group	$ 9,405	$ 10,909
Received from Novartis Pharma AG	—	22,100
Received from Merck & Co., Inc.	4,407	6,262
Other	1,455	902
	$ 15,267	$ 40,173
Long-term portion:		
Received from the sanofi-aventis Group	$ 56,426	$ 65,455
Received from Merck & Co., Inc.	—	3,375
	$ 56,426	$ 68,830

9. Stockholders' Equity

The Company's Amended Certificate of Incorporation provides for the issuance of up to 40 million shares of Class A Stock, par value $0.001 per share, and 160 million shares of Common Stock, par value $0.001 per share. Shares of Class A Stock are convertible, at any time, at the option of the holder into shares of Common Stock on a share-for-share basis. Holders of Class A Stock have rights and privileges identical to Common Stockholders except that Class A Stockholders are entitled to ten votes per share, while Common Stockholders are entitled to one vote per share. Class A Stock may only be transferred to specified Permitted Transferees, as defined. The Company's Board of Directors (the "Board") is authorized to issue up to 30 million shares of preferred stock, in series, with rights, privileges, and qualifications of each series determined by the Board.

During 1996, the Company adopted a Shareholder Rights Plan in which Rights were distributed as a dividend at the rate of one Right for each share of Common Stock and Class A Stock (collectively, "Stock") held by shareholders of record as of the close of business on October 18, 1996. Each Right initially entitles the registered holder to buy a unit ("Unit") consisting of one-one thousandth of a share of Series A Junior Participating Preferred Stock ("A Preferred Stock") at a purchase price of $120 per Unit (the "Purchase Price"). Initially the Rights were attached to all Stock certificates representing shares then outstanding, and no separate Rights certificates were distributed. The Rights will separate from the Stock and a "distribution date" will occur upon the earlier of (i) ten days after a public announcement that a person or group of affiliated or associated persons, excluding certain defined persons, (an "Acquiring Person") has acquired, or has obtained the right to acquire, beneficial ownership of 20% or more of the outstanding shares of Stock or (ii) ten business days following the commencement of a tender offer or exchange offer that would result in a person or group beneficially owning 20% or more of such outstanding shares of Stock. The Rights are not exercisable unless a distribution date occurs and will expire at the close of business on October 18, 2006 unless earlier redeemed by the Company, subject to certain defined restrictions, for $.01 per Right. In the event that an Acquiring Person becomes the beneficial owner of 20% or more of the then outstanding shares of Stock (unless such acquisition is made pursuant to a tender or exchange offer for all outstanding shares of the Company, at a price determined by a majority of the independent directors of the Company who are not representatives, nominees, affiliates, or associates of an Acquiring Person to be fair and otherwise in the best interest of the Company and its shareholders after receiving advice from one or more investment banking firms), each Right (other than Rights held by the Acquiring Person which shall be voided) will entitle the

holder to purchase, at the Right's then current exercise price, common shares (or, in certain circumstances, cash, property or other securities of the Company) having a value twice the Right's Exercise Price. The Right's Exercise Price is the Purchase Price times the number of shares of Common Stock associated with each Right (initially, one). Upon the occurrence of any such events, the Rights held by an Acquiring Person become null and void. In certain circumstances, a Right entitles the holder to receive, upon exercise, shares of common stock of an acquiring company having a value equal to two times the Right's Exercise Price.

As a result of the Shareholder Rights Plan, the Company's Board designated 100,000 shares of preferred stock as A Preferred Stock. The A Preferred Stock has certain preferences, as defined.

In October 2001, the Company completed a private placement of $200.0 million aggregate principal amount of senior subordinated notes, which are convertible into shares of the Company's Common Stock. See Note 10d.

In March 2003, Novartis Pharma AG purchased $48.0 million of newly issued unregistered shares of the Company's Common Stock. Regeneron issued 2,400,000 shares of Common Stock to Novartis in March 2003 and an additional 5,127,050 shares in May 2003 for a total of 7,527,050 shares based upon the average closing price of the Common Stock for the 20 consecutive trading days ending May 12, 2003. See Note 11b.

In August 2003, Regeneron issued to Merck & Co., Inc., 109,450 newly issued unregistered shares of the Company's Common Stock as consideration for a non-exclusive license agreement granted by Merck to the Company. In August 2004, the Company repurchased these shares from Merck for a purchase price of $0.9 million based on the fair market value of the shares on August 19, 2004. The shares were subsequently retired. See Note 10e.

In September 2003, Aventis purchased 2,799,552 newly issued unregistered shares of the Company's Common Stock for $45.0 million, based upon the average closing price of the Common Stock for the five consecutive trading days ending September 4, 2003. See Note 11a

10. Commitments and Contingencies

a. Operating Leases

The Company leases and subleases laboratory and office facilities in Tarrytown, New York under operating lease agreements which expire through December 2009 and contain renewal options for lease extensions on certain facilities through December 2014. The Company also leases manufacturing, office, and warehouse facilities in Rensselaer, New York under an operating lease agreement which expires in July 2007 and contains renewal options to extend the lease for two additional five-year terms and a purchase option. The leases provide for base rent plus additional rental charges for utilities, taxes, and operating expenses, as defined.

The Company leases certain laboratory and office equipment under operating leases which expire at various times through 2007.

REGENERON PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS — (Continued)
(Unless otherwise noted, dollars in thousands, except per share data)

At December 31, 2004, the future minimum noncancelable lease commitments under operating leases were as follows:

December 31,	Facilities	Equipment	Total
2005	$ 4,627	$ 228	$ 4,855
2006	4,539	130	4,669
2007	4,537	22	4,559
2008	1,800		1,800
2009	1,800		1,800
	$ 17,303	$ 380	$ 17,683

Rent expense under operating leases was:

Year Ending December 31,	Facilities	Equipment	Total
2004	$ 5,351	$ 303	$ 5,654
2003	5,394	305	5,699
2002	4,556	257	4,813

In addition to its rent expense for various facilities, the Company paid additional rental charges for utilities, real estate taxes, and operating expenses of $6.0 million, $6.0 million, and $3.6 million for the years ended December 31, 2004 2003, and 2002, respectively.

b. Capital Leases

In 2003 and prior years, the Company had leased equipment under noncancelable capital leases. Lease terms were generally four years after which, for certain leases, the Company purchased the equipment at amounts defined by the agreements. As of December 31, 2003, the Company had no remaining capital leases outstanding.

c. Loan Payable

In March 2003, the Company entered into a collaboration agreement with Novartis Pharma AG. In accordance with that agreement, Regeneron funded its share of 2003 collaboration development expenses through a loan from Novartis, which bore interest at a rate per annum equal to the LIBOR rate plus 2.5%, compounded quarterly. In March 2004, Novartis forgave its outstanding loan to Regeneron totaling $17.8 million, including accrued interest, based on Regeneron's achieving a pre-defined development milestone. See Note 11b.

d. Convertible Debt

In October 2001, the Company issued $200.0 million aggregate principal amount of convertible senior subordinated notes ("Notes") in a private placement for proceeds to the Company of $192.7 million, after deducting the initial purchasers' discount and out-of-pocket expenses (collectively, "Deferred Financing Costs"). The Notes bear interest at 5.5% per annum, payable semi-annually, and mature on October 17, 2008. Deferred Financing Costs, which are included in other assets, are amortized as interest expense over the period from the Notes' issuance to stated maturity. The Notes are convertible, at the option of the holder at any time, into shares of the Company's Common Stock at a conversion price of approximately $30.25 per share, subject to adjustment in certain circumstances. Regeneron may also redeem some or all of the Notes at any time if the closing price of the Company's Common Stock has exceeded 140% of the conversion price then in effect for a

specified period of time. The fair market value of the Notes fluctuates over time. The estimated fair value of the Notes at December 31, 2004 was approximately $190.0 million.

With respect to the Notes, the Company pledged as collateral $31.6 million of U.S. government securities ("Restricted Marketable Securities") which matured at various dates through October 2004. At December 31, 2003, the balance of the Restricted Marketable Securities had an amortized cost basis of $10.9 million, due to scheduled interest payments made on the Notes in 2002 and 2003. Upon maturity, the proceeds of the remaining Restricted Marketable Securities paid the scheduled 2004 interest payments on the Notes when due. The Company considered its Restricted Marketable Securities to be "held-to-maturity," as defined by Statement of Financial Accounting Standards No. 115, *Accounting for Certain Investments in Debt and Equity Securities*. These securities were reported at their amortized cost, which included the direct costs to acquire the securities, plus the amortization of any discount or premium, and accrued interest earned on the securities. The fair value of the Restricted Marketable Securities at December 31, 2003, which was estimated based on quoted market prices, was $11.0 million and the gross unrealized holding gain was $0.1 million. At December 31, 2004 there were no remaining Restricted Marketable Securities.

e. Research Collaboration and Licensing Agreements

As part of the Company's research and development efforts, the Company enters into research collaboration and licensing agreements with related and unrelated companies, scientific collaborators, universities, and consultants. The Company also has a license and supply agreement with Nektar Therapeutics for a reagent used to formulate one of the Company's product candidates. These agreements contain varying terms and provisions which include fees and milestones to be paid by the Company, services to be provided, and ownership rights to certain proprietary technology developed under the agreements. Some of the agreements contain provisions which require the Company to pay royalties, as defined, at rates that range from 0.25% to 10%, in the event the Company sells or licenses any proprietary products developed under the respective agreements.

Certain agreements under which the Company is required to pay fees permit the Company, upon 30 to 90-day written notice, to terminate such agreements. With respect to payments associated with these agreements, the Company incurred expenses of $1.4 million, $2.7 million, and $1.7 million for the years ended December 31, 2004, 2003, and 2002, respectively.

In August 2003, Merck & Co., Inc. granted the Company a non-exclusive license agreement to certain patents and patent applications which may be used in the development and commercialization of AXOKINE®. As consideration, the Company issued to Merck 109,450 newly issued unregistered shares of its Common Stock (the "Merck Shares"), valued at $1.5 million based on the fair market value of shares of the Company's Common Stock on the agreement's effective date. In August 2004, the Company repurchased from Merck and subsequently retired the Merck Shares for $0.9 million based on the fair market value of the shares on August 19, 2004. The Company also made a cash payment of $0.6 million to Merck as required under the license agreement. The agreement also requires the Company to make an additional payment to Merck upon receipt of marketing approval for a product covered by the licensed patents. In addition, the Company would be required to pay royalties, at staggered rates in the mid-single digits, based on the net sales of products covered by the licensed patents.

11. Research and Development Agreements

The Company has entered into various agreements related to its activities to develop and commercialize product candidates and utilize its technology platforms. Amounts earned by the Company in connection with these agreements, which were recognized as contract research and development revenue, research progress payments, or other contract income, as applicable, totaled $198.7 million, $47.4 million, and $10.9 million in

2004, 2003, and 2002, respectively. Total Company incurred expenses associated with these agreements, which include reimbursable, as applicable, and non-reimbursable amounts and an allocable portion of general and administrative costs, were $75.3 million, $56.0 million and $11.9 million in 2004, 2003, and 2002, respectively. Significant agreements are described below.

a. The sanofi-aventis Group

In September 2003, the Company entered into a collaboration agreement (the "s-a Agreement") with the sanofi-aventis Group, to jointly develop and commercialize the Company's Vascular Endothelial Growth Factor ("VEGF") Trap throughout the world with the exception of Japan, where product rights remain with Regeneron. In connection with this agreement, sanofi-aventis made a non-refundable up-front payment of $80.0 million and purchased 2,799,552 newly issued unregistered shares of the Company's Common Stock for $45.0 million, based upon the average closing price of the Common Stock for the five consecutive trading days ending September 4, 2003.

In January 2005, the Company and sanofi-aventis amended the s-a Agreement to exclude local administration of the VEGF Trap to the eye (the "Excluded Field") from joint development under the agreement, and product rights to the VEGF Trap in the Excluded Field reverted to Regeneron. In connection with this amendment, sanofi-aventis made a $25.0 million non-refundable payment to Regeneron (the "Excluded Field Termination Payment") in January 2005.

Under the s-a Agreement, as amended, Regeneron and sanofi-aventis will share co-promotion rights and profits on sales, if any, of the VEGF Trap, except for sales in the Excluded Field. In December 2004, Regeneron earned a $25.0 million payment from sanofi-aventis, which was received in January 2005, upon achievement of an early-stage clinical milestone. The Company 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.

Under the s-a Agreement, agreed upon development expenses incurred by both companies during the term of the agreement will be funded by sanofi-aventis. If the collaboration becomes profitable, Regeneron will reimburse sanofi-aventis for 50% of these development expenses, or half of $86.5 million as of December 31, 2004, in accordance with a formula based on the amount of development expenses and Regeneron's share of the collaboration profits, or at a faster rate at Regeneron's option. Regeneron has the option to conduct additional pre-Phase III studies at its own expense. In connection with the January 2005 amendment to the s-a Agreement, the Excluded Field Termination Payment of $25.0 million will be considered a VEGF Trap development expense and will be subject to 50% reimbursement by Regeneron to sanofi-aventis, as described above, if the collaboration becomes profitable. In addition, if the first commercial sale of a VEGF Trap product in the Excluded Field ("First Excluded Sale") predates the first commercial sale of a VEGF Trap product under the collaboration ("First Collaboration Sale"), Regeneron will begin reimbursing sanofi-aventis for up to $7.5 million of VEGF Trap development expenses, commencing two years after the First Excluded Sale in accordance with a defined formula, until the First Collaboration Sale occurs.

Sanofi-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, Regeneron's obligation to reimburse sanofi-aventis, for 50% of VEGF Trap development expenses will terminate, and the Company will retain all rights to the VEGF Trap.

Revenue related to payments from sanofi-aventis is being recognized under the Substantive Milestone Method (see Note 2) in accordance with SAB 104. The up-front payment of $80.0 million and reimbursement of Regeneron-incurred development expenses are being recognized as contract research and development revenue over the development period. Milestone payments are recognized as research progress payments. In addition to the $25.0 million research progress payment earned in 2004, the Company

recognized $78.3 million and $14.3 million of contract research and development revenue in 2004 and 2003, respectively, in connection with the s-a Agreement. At December 31, 2004 and 2003, amounts receivable from sanofi-aventis totaled $39.4 million and $8.9 million, respectively, and deferred revenue was $65.8 million and $76.4 million, respectively.

b. Novartis Pharma AG

In March 2003, the Company entered into a collaboration agreement (the "Novartis Agreement") with Novartis Pharma AG to jointly develop and commercialize the Company's Interleukin-1 Cytokine Trap ("IL-1 Trap"). In connection with this agreement, Novartis made a non-refundable up-front payment of $27.0 million and purchased $48.0 million of newly issued unregistered shares of the Company's Common Stock. Regeneron issued 2,400,000 shares of Common Stock to Novartis in March 2003 and an additional 5,127,050 shares in May 2003 for a total of 7,527,050 shares based upon the average closing price of the Common Stock for the 20 consecutive trading days ending May 12, 2003.

Development expenses incurred during 2003 were shared equally by the Company and Novartis. Regeneron funded its share of 2003 development expenses through a loan (the "2003 Loan") from Novartis, which bore interest at a rate per annum equal to the LIBOR rate plus 2.5%, compounded quarterly. As of December 31, 2003, the 2003 Loan balance due Novartis, including accrued interest, totaled $13.8 million. In March 2004, Novartis forgave the 2003 Loan and accrued interest thereon, totaling $17.8 million, based on Regeneron's achieving a pre-defined development milestone.

In February 2004, Novartis provided notice of its intention not to proceed with the joint development of the IL-1 Trap. In March 2004, Novartis agreed to pay the Company $42.75 million to satisfy its obligation to fund development costs for the IL-1 Trap for the nine month period following its notification and for the two months prior to that notice. The Company recorded the $42.75 million as other contract income in 2004. Regeneron and Novartis each retain rights under the collaboration agreement to elect to collaborate in the future on the development and commercialization of certain other IL-1 antagonists.

Revenue related to payments from Novartis was recognized under the Substantive Milestone Method (see Note 2) in accordance with SAB 104. The up-front payment of $27.0 million and reimbursement of Novartis' share of Regeneron-incurred development expenses were recognized as contract research and development revenue. Forgiveness of the 2003 Loan and accrued interest in 2004 was recognized as a research progress payment. In 2003 the Company recognized $21.4 million of contract research and development revenue in connection with the Novartis Agreement. At December 31, 2003, amounts receivable from Novartis totaled $3.2 million and deferred revenue was $22.1 million. In 2004, the Company recognized contract research and development revenue of $22.1 million, which represented the remaining amount of the $27.0 million up-front payment from Novartis that had previously been deferred. At December 31, 2004 there were no amounts receivable from Novartis and no deferred revenue.

c. Amgen Inc.

In August 1990, the Company entered into a collaboration agreement (the "Amgen Agreement") with Amgen Inc. to develop and attempt to commercialize two proprietary products (the "Products"). The Amgen Agreement, among other things, provided for Amgen and the Company to form a partnership ("Amgen-Regeneron Partners" or the "Partnership") to complete the development and to commercialize the Products. Amgen and the Company hold equal ownership interests (subject to adjustment for any future inequities in capital contributions, as defined) in the Partnership. The Company accounts for its investment in the Partnership in accordance with the equity method of accounting. In 2004, 2003, and 2002, the Company recognized its share of the Partnership net income (loss) in the amounts of $134 thousand, ($63 thousand), and ($27 thousand), respectively, which represents 50% of the total Partnership net income (loss). In September 2002, the Company and Amgen each made capital withdrawals of $0.5 million from the

Partnership. At December 31, 2004, the Company continues to be an equal partner in Amgen-Regeneron Partners. Selected financial data of the Partnership as of and for the years ended December 31, 2004, 2003, and 2002 are not significant. The Partnership has no ongoing development activities at this time.

In October 2000, Amgen and Regeneron entered into an agreement whereby Regeneron acquired Amgen's patents and patent applications relating to ciliary neurotrophic factor ("CNTF") and related molecules for $1.0 million. As part of this agreement, Regeneron granted back to Amgen exclusive, royalty free rights under these patents and patent applications solely for human ophthalmic uses. In addition, Regeneron entered into a covenant not to sue Amgen under Regeneron's patents and patent applications relating to CNTF and related molecules solely for human ophthalmic uses.

In July 2002, Amgen and Immunex Corporation (now part of Amgen) granted the Company 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 Regeneron 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 the Company 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.

d. Sumitomo Chemical Company, Ltd.

During 1989, Sumitomo Chemical Co., Ltd. entered into a Technology Development Agreement ("TDA") with Regeneron and paid the Company $5.6 million. In consideration for this payment, Sumitomo Chemical received a fifteen year limited right of first negotiation to license up to three of the Company's product candidates in Japan. In connection with the Company's implementation of SAB 101 (see Note 2), the Company recognized this payment as revenue on a straight-line basis over the term of the TDA. The TDA expired in March 2004.

e. The Procter & Gamble Company

In May 1997, the Company entered into a long-term collaboration agreement with The Procter & Gamble Company to discover, develop, and commercialize pharmaceutical products (the "P&G Agreement") and Procter & Gamble agreed to provide funding for Regeneron's research efforts related to the collaboration. In connection with the collaboration, in June 1997 and August 2000, Procter & Gamble purchased 4.35 million and 573,630 shares of the Company's Common Stock at $9.87 and $29.75 per share for a total of $42.9 million and $17.1 million, respectively. In June 1997, Procter & Gamble also received five year warrants to purchase an additional 1.45 million shares of the Company's stock at $9.87 per share, which were exercised in August 2000. As consideration for the exercise price, Procter & Gamble tendered 511,125 shares of the Company's Common Stock which had an aggregate value at the time of exercise, based upon the average market price of the Company's Common Stock over approximately the prior 30 trading days, equal to the aggregate exercise price of the warrants. The net result of this warrant exercise was that Procter & Gamble acquired an additional 938,875 shares of the Company's Common Stock. The 511,125 shares of Common Stock delivered to the Company by Procter & Gamble were retired upon receipt. These equity purchases were in addition to a purchase by Procter & Gamble Pharmaceuticals, Inc. of 800,000 shares of the Company's Common Stock for $10.0 million that was completed in March 1997.

Effective December 31, 2000, the Company and Procter & Gamble entered into a new collaboration agreement, replacing the P&G Agreement. The new agreement extends Procter & Gamble's obligation to fund Regeneron research 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. Under the new agreement, research support from Procter & Gamble is

$2.5 million per quarter, before adjustments for inflation, through December 2005. Any drugs that result from the collaboration will continue to be jointly developed and marketed worldwide, with the companies equally sharing development costs and profits. Procter & Gamble and the Company divided rights to programs from the P&G Agreement that are no longer part of the companies' collaboration. Research funding from Procter & Gamble related to the collaboration totaled $90.8 million through December 31, 2004. In addition, in 1997 through 1999, Procter & Gamble also provided research support for the Company's AXOKINE program and, as a result, will be entitled to receive a small royalty on any sales of AXOKINE.

Contract research and development revenue related to the Company's collaboration with Procter & Gamble was $10.5 million, $10.6 million, and $10.5 million in 2004, 2003, and 2002, respectively. At December 31, 2004, 2003, and 2002, the Procter & Gamble contract research revenue receivable was $2.3 million, $2.7 million, and $2.6 million, respectively.

f. Serono, S.A.

In December 2002, the Company entered into an agreement (the "Serono Agreement") with Serono S.A. to use Regeneron's proprietary Velocigene technology platform to provide Serono with knock-out and transgenic mammalian models of gene function ("Materials"). Serono made an advance payment of $1.5 million (the "Retainer") to Regeneron in December 2002, which was accounted for as deferred revenue. Regeneron recognizes revenue and reduces the Retainer as Materials are shipped to and accepted by Serono. The Serono Agreement contains provisions for minimum yearly order quantities and replenishment of the Retainer when the balance declines below a specified threshold. In 2004 and 2003, the Company recognized $2.1 million and $0.7 million, respectively, of contract research and development revenue in connection with the Serono Agreement.

12. Manufacturing Agreement

During 1995, the Company entered into a long-term manufacturing agreement with Merck & Co., Inc., as amended, (the "Merck Agreement") to produce an intermediate (the "Intermediate") for a Merck pediatric vaccine at the Company's Rensselaer, New York facility. The Company agreed to modify portions of its facility for manufacture of the Intermediate and to assist Merck in securing regulatory approval for such manufacture in the Company's facility. The Merck Agreement calls for the Company to manufacture Intermediate for Merck for a specified period of time (the "Production Period"), with certain minimum order quantities each year. The Production Period commenced in November of 1999 and originally extended for six years. In February 2005, the Company and Merck amended the Merck Agreement to extend the Production Period through October 2006 and provide Merck an opportunity, upon twelve-months' prior notice, to extend the Production Period for an additional year through October 2007. Merck may terminate the agreement at any time upon the payment by Merck of a termination fee.

Merck agreed to reimburse the Company for the capital costs to modify the facility ("Capital Costs"). Merck also agreed to pay an annual facility fee (the "Facility Fee") of $1.0 million beginning March 1995, subject to annual adjustment for inflation. During the Production Period, Merck agreed to reimburse the Company for certain manufacturing costs, pay the Company a variable fee based on the quantity of Intermediate supplied to Merck, and make additional bi-annual payments ("Additional Payments"), as defined. In addition, Merck agreed to reimburse the Company for the cost of Company activities performed on behalf of Merck prior to the Production Period and for miscellaneous costs during the Production Period ("Internal Costs"). These payments are recognized as contract manufacturing revenue as follows: (i) payments for Internal Costs are recognized as the activities are performed, (ii) the Facility Fee and Additional Payments are recognized over the period to which they relate, (iii) payments for Capital Costs were deferred and are recognized as Intermediate is shipped to Merck, and (iv) payments related to the

manufacture of Intermediate during the Production Period ("Manufacturing Payments") are recognized after the Intermediate is tested and approved by, and shipped (FOB Shipping Point) to, Merck.

In 2004, 2003, and 2002, Merck contract manufacturing revenue totaled $18.1 million, $10.1 million, and $11.1 million, respectively. Such amounts include $3.6 million, $1.7 million, and $1.8 million of previously deferred Capital Costs, respectively. In addition, Merck contract manufacturing revenue for 2002 includes a non-recurring $1.0 million payment received in August 2002 related to services the Company provided in prior years.

13. Incentive and Stock Purchase Plans

a. Long-Term Incentive Plans

During 2000, the Company established the Regeneron Pharmaceuticals, Inc. 2000 Long-Term Incentive Plan ("2000 Incentive Plan") which, as amended, provides for the issuance of up to 18,500,000 shares of Common Stock in respect of awards. In addition, shares of Common Stock previously approved by shareholders for issuance under the Regeneron Pharmaceuticals, Inc. 1990 Long-Term Incentive Plan ("1990 Incentive Plan") that are not issued under the 1990 Incentive Plan, may be issued as awards under the 2000 Incentive Plan. Employees of the Company, including officers, and nonemployees, including consultants and nonemployee members of the Board of Directors, (collectively, "Participants") may receive awards as determined by a committee of independent directors ("Committee"). The awards that may be made under the 2000 Incentive Plan include: (a) Incentive Stock Options ("ISOs") and Nonqualified Stock Options, (b) shares of Restricted Stock, (c) shares of Phantom Stock, (d) Stock Bonuses, and (e) Other Awards.

Stock Option awards grant Participants the right to purchase shares of Common Stock at prices determined by the Committee; however, in the case of an ISO, the option exercise price will not be less than the fair market value of a share of Common Stock on the date the Option is granted. Options vest over a period of time determined by the Committee, generally on a pro rata basis over a three to five year period. The Committee also determines the expiration date of each Option; however, no ISO is exercisable more than ten years after the date of grant.

Restricted Stock awards grant Participants shares of restricted Common Stock or allow Participants to purchase such shares at a price determined by the Committee. Such shares are nontransferable for a period determined by the Committee ("vesting period"). Should employment terminate, as defined by the 2000 Incentive Plan, the ownership of the Restricted Stock, which has not vested, will be transferred to the Company, except under defined circumstances with Committee approval, in consideration of amounts, if any, paid by the Participant to acquire such shares. In addition, if the Company requires a return of the Restricted Shares, it also has the right to require a return of all dividends paid on such shares.

Phantom Stock awards provide the Participant the right to receive, within 30 days of the date on which the share vests, an amount, in cash and/or shares of the Company's Common Stock as determined by the Committee, equal to the sum of the fair market value of a share of Common Stock on the date such share of Phantom Stock vests and the aggregate amount of cash dividends paid with respect to a share of Common Stock during the period from the grant date of the share of Phantom Stock to the date on which the share vests. Stock Bonus awards are bonuses payable in shares of Common Stock which are granted at the discretion of the Committee.

Other Awards are other forms of awards which are valued based on the Company's Common Stock. Subject to the provisions of the 2000 Incentive Plan, the terms and provisions of such Other Awards are determined solely on the authority of the Committee.

During 1990, the Company established the 1990 Incentive Plan which, as amended, provided for a maximum of 6,900,000 shares of Common Stock in respect of awards. Employees of the Company, including

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officers, and nonemployees, including consultants and nonemployee members of the Board of Directors, received awards as determined by a committee of independent directors. Under the provisions of the 1990 Incentive Plan, there will be no future awards from the plan. Awards under the 1990 Incentive Plan consisted of Incentive Stock Options and Nonqualified Stock Options which generally vest on a pro rata basis over a three or five year period and have a term of ten years.

The 1990 and 2000 Incentive Plans contain provisions that allow for the Committee to provide for the immediate vesting of awards upon a change in control of the Company, as defined.

The Company may incur charges to operations in connection with awards from these Incentive Plans. In accordance with APB No. 25 and related interpretations, the Company will record compensation expense from employee stock-based awards under certain conditions. Generally, when the terms of the award and the amount the employee must pay to acquire the stock are fixed, compensation expense for options, restricted stock, and stock bonus awards will total the grant date intrinsic value, if any, amortized over the vesting period. For other awards, including phantom stock, compensation expense will be recognized over the life of the award based on the cash remitted to settle the award or the intrinsic value of the award on the date of exercise.

Transactions involving stock option awards during 2004, 2003, and 2002, under the 1990 and 2000 Incentive Plans, are summarized in the table below. Option exercise prices were greater than or equal to the fair market value of the Company's Common Stock on the date of grant. The total number of options exercisable at December 31, 2004, 2003, and 2002 was 8,628,873, 5,940,268, and 4,670,695, respectively, with weighted average exercise prices of $21.05, $19.45, and $15.80, respectively.

	Number of Shares	Weighted-Average Exercise Price
Stock options outstanding at December 31, 2001	9,328,039	$ 21.10
2002:		
Stock options granted	2,693,010	$ 19.97
Stock options canceled	(183,031)	$ 22.63
Stock options exercised	(274,068)	$ 9.96
Stock options outstanding at December 31, 2002	11,563,950	$ 21.08
2003:		
Stock options granted	2,634,570	$ 13.45
Stock options canceled	(265,107)	$ 22.62
Stock options exercised	(795,114)	$ 7.07
Stock options outstanding at December 31, 2003	13,138,299	$ 20.36
2004:		
Stock options granted	2,828,484	$ 9.90
Stock options canceled	(514,947)	$ 21.10
Stock options exercised	(311,268)	$ 5.98
Stock options outstanding at December 31, 2004	15,140,568	$ 18.68

REGENERON PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS — (Continued)
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The following table summarizes stock option information as of December 31, 2004:

	Options Outstanding			Options Exercisable	
Range of Exercise Prices	Number Outstanding	Weighted Average Remaining Contractual Life	Weighted Average Exercise Price	Number Exercisable	Weighted Average Exercise Price
$ 5.25 to $ 9.49	4,572,718	7.22	$ 8.78	2,070,420	$ 8.00
$ 9.50 to $13.00	3,282,599	7.07	$ 12.36	1,693,510	$ 11.88
$13.05 to $23.29	2,624,114	7.97	$ 18.86	1,338,769	$ 19.30
$23.66 to $28.81	2,551,117	6.67	$ 27.30	1,725,554	$ 27.61
$28.84 to $50.38	2,049,520	5.86	$ 38.94	1,740,220	$ 39.30
$51.56 to $51.56	60,500	5.16	$ 51.56	60,400	$ 51.56
$ 5.25 to $51.56	15,140,568	7.03	$ 18.68	8,628,873	$ 21.05

The effect on the Company's net loss and net loss per share had compensation costs for the Incentive Plans been determined in accordance with the fair value based method of accounting for stock-based compensation as prescribed by SFAS No. 123 is shown in Note 2. For the purpose of the pro forma calculation, the fair value of each option granted from the Incentive Plans during 2004, 2003, and 2002 was estimated on the date of grant using the Black-Scholes option-pricing model. The weighted-average fair value of the options granted during 2004, 2003, and 2002 was $7.53, $10.12 and $14.10, respectively. The following table summarizes the assumptions used in computing the fair value of option grants.

	2004	2003	2002
Expected volatility	80%	80%	70%
Expected lives from vest date	5 years	5 years	5 years
Dividend yield	0%	0%	0%
Risk-free interest rate	4.03%	3.75%	4.34%

During 2004, 2003, and 2002, 105,052, 219,367, and 139,611 shares, respectively, of Restricted Stock were awarded under the 2000 Incentive Plan. These shares are nontransferable with such restriction lapsing (i) for 2004 awards with respect to 50% of the shares at nine months and eighteen months from date of grant and (ii) for 2003 and 2002 awards with respect to 25% of the shares every six months over the two-year period from date of grant. In accordance with generally accepted accounting principles, the Company recorded unearned compensation within Stockholders' Equity of $1.0 million, $2.9 million, and $2.7 million in 2004, 2003, and 2002, respectively, related to these awards. This amount was based on the fair market value of shares of the Company's Common Stock on the date of grant and will be expensed, on a pro rata basis, over the period that the restriction on these shares lapses. During 2004, 2003, and 2002, 18,194, 4,431, and 2,183 shares, respectively, of Restricted Stock were forfeited due to employee terminations. The Company reduced unearned compensation within Stockholders' Equity by $0.3 million, $0.1 million, and $0.1 million in 2004, 2003, and 2002, respectively, related to these forfeited awards.

The Company recognized compensation expense from stock-based awards of $2.5 million $2.3 million, and $1.8 million in 2004, 2003, and 2002, respectively.

As of December 31, 2004, there were 5,553,915 shares available for future grants under the 2000 Incentive Plan.

In December 2004, the Company's shareholders approved a stock option exchange program. Under the program, Company regular employees who work an average of 20 hours per week, other than the Company's chairman and the Company's president and chief executive officer, were provided the opportunity to make a

(Unless otherwise noted, dollars in thousands, except per share data)

one-time election to surrender options granted under the 1990 and 2000 Incentive Plans that had an exercise price per share of at least $18.00 and exchange them for replacement options granted under the 2000 Incentive Plan in accordance with the following exchange ratios:

Exercise Price of Eligible Options	Exchange Ratio (Number of Eligible Options to be Surrendered and Cancelled for Each Replacement Option)
$18.00 to $28.00	1.50
$28.01 to $37.00	2.00
$37.01 and up	3.00

Participation in the stock option exchange program was voluntary, and non-employee directors, consultants, former employees, and retirees were not eligible to participate. The participation deadline for the program was January 5, 2005. Eligible employees elected to exchange options with a total of 3,665,819 underlying shares of Common Stock, and the Company issued 1,977,840 replacement options with an exercise price of $8.50 per share on January 5, 2005.

  Each replacement option was completely unvested upon grant. Each replacement option granted to an employee other than our executive vice president and senior vice presidents will ordinarily become vested and exercisable with respect to one-fourth of the shares initially underlying such option on each of the first, second, third and fourth anniversaries of the grant date so that such replacement option will be fully vested and exercisable four years after it was granted. Each replacement option granted to our executive vice president and senior vice presidents will ordinarily vest with respect to all the shares underlying such option if both (i) the Company's products have achieved gross sales of at least $100 million during any consecutive twelve-month period (either directly by the Company or through its licensees) and (ii) the specific senior or executive vice president has remained employed by the Company for at least three years from the date of grant. For all replacement options, the recipient's vesting and exercise rights are contingent upon the recipient's continued employment through the applicable vesting date and subject to the other terms of the 2000 Incentive Plan and the applicable option award agreement. As is generally the case with respect to the option award agreements for options that were eligible for exchange pursuant to the stock option exchange program, the option award agreements for replacement options include provisions whereby the replacement options may become fully vested in connection with a "Change in Control" of the Company, as defined in the 2000 Incentive Plan.

Under the stock option exchange program, each replacement option has a term equal to the greater of (i) the remaining term of the surrendered option it replaces and (ii) six years from the date of grant of the replacement option. This was intended to ensure that the employees who participated in the stock option exchange program would not derive any additional benefit from an extended option term unless the surrendered option had a remaining term of less than six years.

In connection with the stock option exchange program, the Company intends to adopt, effective January 1, 2005, the fair value based method of accounting for stock-based employee compensation under the provisions of SFAS No. 123, as modified by SFAS No. 148, using the modified prospective method. In accordance with SFAS Nos. 123/148, as a result of the Company's grant of the replacement options pursuant to the stock option exchange program, the Company incurred compensation cost that will be recognized over the vesting period of the replacement option. The compensation cost equals the sum of (i) the unamortized fair value of the surrendered options on the date of the exchange and (ii) the incremental value of the replacement option measured as the difference between (a) the fair value of the replacement option on the date of the exchange and (b) the fair value of the surrendered options immediately prior to the exchange. The

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Company will begin recognizing this compensation cost in the first quarter of 2005 in each of the categories of expense in the Company's Statement of Operations.

b. Executive Stock Purchase Plan

In 1989, the Company adopted an Executive Stock Purchase Plan (the "Plan") under which 1,027,500 shares of Class A Stock were reserved for restricted stock awards. The Plan provides for the compensation committee of the Board of Directors to award employees, directors, consultants, and other individuals ("Plan participants") who render service to the Company the right to purchase Class A Stock at a price set by the compensation committee. The Plan provides for the vesting of shares as determined by the compensation committee and, should the Company's relationship with a Plan participant terminate before all shares are vested, unvested shares will be repurchased by the Company at a price per share equal to the original amount paid by the Plan participant. During 1989 and 1990, a total of 983,254 shares were issued, all of which vested as of December 31, 1999. As of December 31, 2004, there were 44,246 shares available for future grants under the Plan.

14. Employee Savings Plan

In 1993, the Company adopted the provisions of the Regeneron Pharmaceuticals, Inc. 401(k) Savings Plan (the "Savings Plan"). The terms of the Savings Plan provide for employees who have met defined service requirements to participate in the Savings Plan by electing to contribute to the Savings Plan a percentage of their compensation to be set aside to pay their future retirement benefits, as defined. The Savings Plan, as amended and restated during 1998, provides for the Company to make discretionary contributions ("Contribution"), as defined. The Company recorded Contribution expense of $0.8 million in 2004, $0.9 million in 2003, and $0.8 million in 2002; such amounts were accrued as liabilities at December 31, 2004, 2003, and 2002, respectively. During the first quarter of 2005, 2004, and 2003, the Company contributed 90,385, 64,333, and 42,543 shares, respectively, of Common Stock to the Savings Plan in satisfaction of these obligations.

15. Income Taxes

In 2004, 2003, and 2002, the Company recognized a net operating loss for tax purposes and, accordingly, no provision for income taxes has been recorded in the accompanying financial statements. There is no benefit for federal or state income taxes for the years ended December 31, 2004, 2003, and 2002 since the Company has incurred net operating losses for tax purposes since inception and established a valuation allowance equal to the total deferred tax asset.

The tax effect of temporary differences, net operating loss carry-forwards, and research and experimental tax credit carry-forwards as of December 31, 2004 and 2003 was as follows:

	2004	2003
Deferred tax assets		
Net operating loss carry-forward	$ 135,099	$ 135,357
Fixed assets	9,772	7,177
Deferred revenue	28,527	43,372
Research and experimental tax credit carry-forward	20,772	18,233
Capitalized research and development costs	28,559	33,102
Other	4,168	3,832
Valuation allowance	(226,897)	(241,073)
	—	—

For all years presented, the Company's effective income tax rate is zero. The difference between the Company's effective income tax rate and the Federal statutory rate of 34% is attributable to state tax benefits and tax credit carry-forwards offset by an increase in the deferred tax valuation allowance.

As of December 31, 2004, the Company had available for tax purposes unused net operating loss carry-forwards of $339.5 million which will expire in various years from 2006 to 2024. The Company's research and experimental tax credit carry-forwards expire in various years from 2005 to 2024. Under the Internal Revenue Code and similar state provisions, substantial changes in the Company's ownership have resulted in an annual limitation on the amount of net operating loss and tax credit carry-forwards that can be utilized in future years to offset future taxable income. This annual limitation may result in the expiration of net operating losses and tax credit carry-forwards before utilization.

16. Legal Matters

In May 2003, securities class action lawsuits were commenced against Regeneron and certain of the Company's 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 the Company's 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. The ultimate outcome of this matter cannot presently be determined. Accordingly, no provision for any liability that may result upon the resolution of this matter has been made in the accompanying financial statements.

The Company, from time to time, has been subject to other legal claims arising in connection with its business. While the ultimate outcome of these other legal claims cannot be predicted with certainty, at December 31, 2004 there were no such other asserted claims against the Company which, in the opinion of management, if adversely determined would have a material adverse effect on the Company's financial position, results of operations, and cash flows.

17. Net Income (Loss) Per Share

The Company's basic net income (loss) per share amounts have been computed by dividing net income (loss) by the weighted average number of Common and Class A shares outstanding. The diluted net income per share is based upon the weighted average number of shares of Common Stock and Class A Stock and the common stock equivalents outstanding when dilutive. In 2003 and 2002, the Company reported net losses and, therefore, no common stock equivalents were included in the computation of diluted net loss per share since

such inclusion would have been antidilutive. The calculations of basic and diluted net loss per share are as follows:

	December 31,		
	2004	2003	2002
Net income (loss) (Numerator)	$ 41,699	$ (107,458)	$ (124,377)
Shares, in thousands (Denominator):			
Weighted-average shares for basic per share calculations	55,419	50,490	43,918
Effect of stock options	711		
Effect of restricted stock awards	42	—	—
Adjusted weighted-average shares for diluted per share calculations	56,172	50,490	43,918
Basic net income (loss) per share	$ 0.75	$ (2.13)	$ (2.83)
Diluted net income (loss) per share	$ 0.74	$ (2.13)	$ (2.83)

Shares issuable upon the exercise of options and warrants, vesting of restricted stock awards, and conversion of convertible debt, which have been excluded from the diluted per share amounts because their effect would have been antidilutive, include the following:

	December 31,		
	2004	2003	2002
Options and Warrants:			
Weighted average number, in thousands	10,110	11,299	9,533
Weighted average exercise price	$ 23.82	$ 22.07	$ 19.43
Restricted Stock:			
Weighted average number, in thousands	6	159	88
Convertible Debt:			
Weighted average number, in thousands	6,611	6,611	6,611
Conversion price	$ 30.25	$ 30.25	$ 30.25

In connection with the Company's stock option exchange program (see Note 13a), on January 5, 2005, eligible employees elected to exchange options with a total of 3,665,819 underlying shares of Common Stock, and the Company issued 1,977,840 replacement options with an exercise price of $8.50 per share.

18. Segment Information

The Company's operations are managed in two business segments: research and development, and contract manufacturing.

Research and development: Includes all activities related to the discovery of potential therapeutics for human medical conditions, and the development and commercialization of these discoveries. Also includes revenues and expenses related to (i) the development of manufacturing processes prior to commencing commercial production of a product under contract manufacturing arrangements and (ii) the supply of specified, ordered research materials using Regeneron-developed proprietary technology (see Note 13).

Contract manufacturing: Includes all revenues and expenses related to the commercial production of products under contract manufacturing arrangements. During 2004, 2003, and 2002, the Company produced Intermediate under the Merck Agreement (see Note 12).

REGENERON PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS — (Continued)
(Unless otherwise noted, dollars in thousands, except per share data)

The table below presents information about reported segments for the years ended December 31, 2004, 2003, and 2002:

	Research & Development	Contract Manufacturing	Reconciling Items	Total
2004				
Revenues	$ 155,927	$ 18,090	—	$ 174,017
Depreciation and amortization	14,319	—(1)	$ 1,043	15,362
Interest expense	126	—	12,049	12,175
Other contract income	42,750	—		42,750
Net income (loss)	45,395	2,876	(6,572)(2)	41,699
Capital expenditures	5,972	—	—	5,972
Total assets	111,038	6,532	355,538(3)	473,108
2003				
Revenues	$ 47,366	$ 10,131	—	$ 57,497
Depreciation and amortization	11,894	—(1)	$ 1,043	12,937
Interest expense	161	—	11,771	11,932
Net (loss) income	(103,604)	3,455	(7,309)(2)	(107,458)
Capital expenditures	16,944	—	—	16,944
Total assets	92,369	12,889	374,297(3)	479,555
2002				
Revenues	$ 10,924	$ 11,064	—	$ 21,988
Depreciation and amortization	7,411	—(1)	$ 1,043	8,454
Interest expense	36	2	11,821	11,859
Net (loss) income	(126,597)	4,579	(2,359)(2)	(124,377)
Capital expenditures	45,878	36	—	45,914
Total assets	75,589	12,479	303,506(3)	391,574

(1) Depreciation and amortization related to contract manufacturing is capitalized into inventory and included in contract manufacturing expense when the product is shipped.

(2) Represents investment income net of interest expense related to convertible notes issued in October 2001 (see Note 10d).

(3) Includes cash and cash equivalents, marketable securities, restricted marketable securities (where applicable), prepaid expenses and other current assets, and other assets.

REGENERON PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS — (Continued)
(Unless otherwise noted, dollars in thousands, except per share data)

19. Unaudited Quarterly Results

Summarized quarterly financial data for the years ended December 31, 2004 and 2003 are displayed in the following tables.

	First Quarter Ended March 31, 2004	Second Quarter Ended June 30, 2004	Third Quarter Ended September 30, 2004	Fourth Quarter Ended December 31, 2004
	(Unaudited)	(Unaudited)	(Unaudited)	(Unaudited)
Revenues	$ 61,990	$ 28,418	$ 36,519	$ 47,090
Net income (loss)	64,532	(14,549)	(11,076)	2,792
Basic net income (loss) per share	$ 1.17	$ (0.26)	$ (0.20)	$ 0.05
Diluted net income (loss) per share	$ 1.06	$ (0.26)	$ (0.20)	$ 0.05

	First Quarter Ended March 31, 2003	Second Quarter Ended June 30, 2003	Third Quarter Ended September 30, 2003	Fourth Quarter Ended December 31, 2003
	(Unaudited)	(Unaudited)	(Unaudited)	(Unaudited)
Revenues	$ 9,925	$ 8,908	$ 17,392	$ 21,272
Net loss	(30,321)	(30,360)	(27,400)	(19,377)
Net loss per share, basic and diluted	$ (0.68)	$ (0.61)	$ (0.52)	$ (0.35)

Exhibit 3.2

BY-LAWS

OF

REGENERON PHARMACEUTICALS, INC.

(Amended Through November 12, 2004)

ARTICLE I

SHAREHOLDERS

Section 1. Annual Meeting. The annual meeting of the shareholders of the Corporation shall be held either within or without the State of New York, at such place and at such time as the Board of Directors may designate and set forth in the call or in a waiver of notice thereof, for the purpose of electing directors and for the transaction of such other business as may properly be brought before the meeting, provided that until changed by the Board of Directors, the annual meeting of the shareholders shall be held on the first Monday in June in each year, if not a legal holiday, and if a legal holiday, then on the next business day following, at 10:00 a.m., at which meeting the shareholders shall elect a Board of Directors for the ensuing year and transact such other business as may properly be brought before the meeting.

Section 2. Proposed Business at Annual Meeting. No business may be transacted at an annual meeting of shareholders, other than business that is either (a) specified in the notice of meeting (or any supplement thereto) given by or at the direction of the Board of Directors (or any duly authorized committee thereof), which shall include shareholder proposals contained in the Corporation's proxy statement made in accordance with Rule 14a-8 of the Securities and Exchange Act of 1934, as amended, or any successor thereto, (b) otherwise properly brought before the annual meeting by or at the direction of the Board of Directors (or any duly authorized committee thereof) or (c) otherwise properly brought before the annual meeting by any shareholder of the Company (i) who is a shareholder of record on the date of the giving of the notice provided for in this Section 2 and on the record date for the determination of shareholders entitled to vote at such annual meeting and (ii) who complies with the notice procedures set forth in this Section 2.

In addition to any other applicable requirements, for business to be properly brought before an annual meeting by a shareholder, such shareholder must have given timely notice thereof in proper written form to the Secretary of the Company.

To be timely, a shareholder's notice to the Secretary must be delivered to or mailed and received at the principal executive offices of the

Company not less than sixty (60) days nor more than ninety (90) days prior to the date of the annual meeting; provided, however, that in the event that less than seventy (70) days' notice or prior public disclosure of the date of the annual meeting is given or made to shareholders, notice by the shareholder in order to be timely must be so received not later than the close of business on the tenth (10th) day following the day on which such notice of the date of the annual meeting was mailed or such public disclosure of the date of the annual meeting was made, whichever first occurs.

To be in proper written form, a shareholder's notice to the Secretary must set forth as to each matter such shareholder proposes to bring before the annual meeting (i) a brief description of the business desired to be brought before the annual meeting and the reasons for conducting such business at the annual meeting, (ii) the name and record address of such shareholder, (iii) the class or series and number of shares of capital stock of the Company which are owned beneficially or of record by such shareholder, (iv) a description of all arrangements or understandings between such shareholder and any other person or persons (including their names) in connection with the proposal of such business by such shareholder and any material interest of such shareholder in such business and (v) a representation that such shareholder intends to appear in person or by proxy at the annual meeting to bring such business before the meeting.

No business shall be conducted at the annual meeting of shareholders except business brought before the annual meeting in accordance with the procedures set forth in this Section 2, provided, however, that, once business has been properly brought before the annual meeting in accordance with such procedures, nothing in this Section 2 shall be deemed to preclude discussion by any shareholder of any such business. If the Chairman of an annual meeting determines that business was not properly brought before the annual meeting in accordance with the foregoing procedures, the Chairman shall declare to the meeting that the business was not properly brought before the meeting and such business shall not be transacted.

Section 3. Special Meetings. Special Meetings of the shareholders, for any purpose or purposes, may be called at any time by resolution of the Board of Directors or by the President, and shall be called by the President or by the Secretary upon the written request of the holders of record of shares, issued and outstanding the entitled to cast at least twenty-five percent (25%) of the total number of votes entitled to be cast by shareholders at such meeting, at such times and at such place either within or without the State of New York as may be stated in the call or in a waiver of notice thereof.

Section 4. Notice of Meetings. Notice of the time, place and purpose of every meeting of shareholders shall be delivered personally or by first class mail, not less than ten days nor more than fifty days previous thereto, or by

third class mail, not less than twenty four nor more than fifty days before the meeting, to each shareholder of record entitled to vote, at his post office address appearing upon the records of the Corporation or at such other address as shall be furnished in writing by him to the Corporation for such purpose. Such further notice shall be given as may be required by law or by these By-Laws. Any meeting may be held without notice if all shareholders entitled to vote are present in person or by proxy, or if notice is waived in writing, either before or after the meeting, by those not present.

Section 5. Quorum. The holders of record of at least a majority of the votes of shares of the stock of the Corporation, issued and outstanding and entitled to vote, present in person or by proxy, shall, except as otherwise provided by law, the Certificate of Incorporation or by these By-Laws, constitute a quorum at all meetings of the shareholders; if there be no such quorum, the holders of a majority of the votes of such shares so present or represented may adjourn the meeting from time to time until a quorum shall have been obtained.

Section 6. Organization of Meetings. Meetings of the shareholders shall be presided over by the Chairman of the Board, if there be one, or if he is not present by the President, or if he is not present by a chairman to be chosen at the meeting. The Secretary of the Corporation, or in his absence an Assistant Secretary, shall act as Secretary of the meeting, if present.

Section 7. Voting. At each meeting of shareholders, except as otherwise provided by statute, every holder of record of stock entitled to vote shall be entitled to cast the number of votes to which shares of such class or series are entitled as set forth in the Certificate of Incorporation or any Certificate of Designation with respect to any preferred stock, in person or by proxy for each share of such stock standing in his name on the records of the Corporation. Elections of directors shall be determined by a plurality of the votes cast thereat and, except as otherwise provided by statute, the Certificate of Incorporation, or these By-Laws, all other action shall be determined by a majority of the votes cast at such meeting. Each proxy to vote shall be in writing and signed by the shareholder or by his duly authorized attorney.

At all elections of directors, the voting shall be by ballot or in such other manner as may be determined by the shareholders present in person or by proxy entitled to vote at such election. With respect to any other matter presented to the shareholders for their consideration at a meeting, any shareholder entitled to vote may, on any question, demand a vote by ballot.

A complete list of the shareholders entitled to vote at each such meeting, arranged in alphabetical order, with the address of each shareholder, the number of shares registered in the name of each shareholder, the class or series of such shares and the number of votes which such shares are entitled, shall be prepared by the Secretary and shall be open to the examination of any

shareholder, for any purpose, germane to the meeting, during ordinary business hours, for a period of time of at least ten days prior to the meeting, either at a place within the city where the meeting is to be held, which place shall be specified in the notice of meeting, or, if not so specified, at the place where the meeting is to be held. The list shall also be produced and kept at the time and place of the meeting during the whole time thereof, and may be inspected by any shareholder who is present.

Section 8. Action by Consent. Any action required or permitted to be taken at any meeting of shareholders may be taken without a meeting, if, prior to such action, a written consent or consents thereto setting forth such action, is signed by the holders of record of all of the shares of the stock of the Corporation, issued and outstanding and entitled to vote.

ARTICLE II

DIRECTORS

Section 1. Number, Quorum, Term, Vacancies, Removal. The number of directors of the Corporation shall be fixed in the manner provided in the Certificate of Incorporation.

A majority of the members of the Board of Directors then holding office shall constitute a quorum for the transaction of business, but if at any meeting of the Board there shall be less than a quorum present, a majority of those present may adjourn the meeting from time to time until a quorum shall have been obtained.

Except as otherwise provided in the Certificate of Incorporation, Directors shall hold office until the next annual election at which the class to which a director shall have been elected is scheduled to stand for reelection and until their successors shall have been elected and shall have qualified, unless sooner displaced.

Except as otherwise required by the Certificate of Incorporation, whenever any vacancy shall have occurred in the Board of Directors, by reason of death, resignation, or otherwise, other than removal of a director with cause by a vote of the shareholders as provided in the Certificate of Incorporation, it shall be filled by a majority of the remaining directors, though less than a quorum (except as otherwise provided by law), and the person so chosen shall serve for a term that coincides with the term of the class to which such director shall have been elected and until his successor is duly elected and has qualified.

Any one or more of the directors of the Corporation may be removed with cause at any time by a vote of the shareholders as provided in the

Certificate of Incorporation and thereupon the term of the director or directors who shall have been so removed shall forthwith terminate and there shall be a vacancy or vacancies in the Board of Directors, to be filled by a vote of the directors as provided in these By-Laws.

Section 2. Nomination of Directors. Only persons who are nominated in accordance with the following procedures shall be eligible for election as directors of the Company, except as may be otherwise provided in the Certificate of Incorporation of the Company with respect to the right of holders of certain specified classes of preferred stock of the Company to nominate and elect a specified number of directors in certain circumstances. Nominations of persons for election to the Board of Directors may be made at any annual meeting of shareholders, or at any special meeting of shareholders called for the purpose of electing directors, (a) by or at the direction of the Board of Directors (or any duly authorized committee thereof) or (b) by any shareholder of the Company (i) who is a shareholder of record on the date of the giving of the notice provided for in this Section 2 and on the record date for the determination of shareholders entitled to vote at such meeting and (ii) who complies with the

notice procedures set forth in this Section 2.

In addition to any other applicable requirements, for a nomination to be made by a shareholder, such shareholder must have given timely notice thereof in proper written form to the Secretary of the Company.

To be timely, a shareholder's notice to the Secretary must be delivered to or mailed and received at the principal executive offices of the Company (a) in the case of an annual meeting, not less than sixty (60) days nor more than ninety (90) days prior to the date of the annual meeting; provided, however, that in the event that less than seventy (70) days' notice or prior public disclosure of the date of the annual meeting is given or made to shareholders, notice by the shareholder in order to be timely must be so received not later than the close of business on the tenth (10th) day following the day on which such notice of the date of the annual meeting was mailed or such public disclosure of the date of the annual meeting was made, whichever first occurs; and (b) in the case of a special meeting of shareholders called for the purpose of electing directors, not later than the close of business on the tenth (10th) day following the day on which notice of the date of the special meeting was mailed or public disclosure of the date of the special meeting was made, whichever first occurs.

To be in proper written form, a shareholder's notice to the Secretary must set forth (a) as to each person whom the shareholder proposes to nominate for election as a director (i) the name, age, business address and residence address of the person, (ii) the principal occupation or employment of the person, (iii) the class or series and number of shares of capital stock of the Company which are owned beneficially or of record by the person and (iv) any other information relating to the person that would be required to be disclosed in a

proxy statement or other filings required to be made in connection with solicitations of proxies for election of directors pursuant to Section 14 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and the rules and regulations promulgated thereunder; and (b) as to the shareholder giving the notice (i) the name and record address of such shareholder, (ii) the class or series and number of shares of capital stock of the Company which are owned beneficially or of record by such shareholder, (iii) a description of all arrangements or understandings between such shareholder and each proposed nominee and any other person or persons (including their names) pursuant to which the nomination(s) are to be made by such shareholder, (iv) a representation that such shareholder intends to appear in person or by proxy at the meeting to nominate the persons named in its notice and (v) any other information relating to such shareholder that would be required to be disclosed in a proxy statement or other filings required to be made in connection with solicitations of proxies for election of directors pursuant to Section 14 of the Exchange Act and the rules and regulations promulgated thereunder. Such notice must be accompanied by a written consent of each proposed nominee to being named as a nominee and to serve as a director if elected.

No person shall be eligible for election as a director of the Company unless nominated in accordance with the procedures set forth in this Section 2. If the Chairman of the meeting determines that a nomination was not made in accordance with the foregoing procedures, the Chairman shall declare to the meeting that the nomination was defective and such defective nomination shall be disregarded.

Section 3. Meetings, Notice. Meetings of the Board of Directors shall be held at such place either within or without the State of New York, as may from time to time be fixed by resolution of the Board, or as may be specified in the call or in a waiver of notice thereof. Regular meetings of the Board of Directors shall be held at such times as may from time to time be fixed by resolution of the Board, and special meetings may be held at any time upon the call of one director, the Chairman of the Board, if one be elected, or the President, by oral, telegraphic or written notice, duly served on or sent or mailed to each director not less than two days before such meeting. A meeting of the Board may be held without notice immediately after the annual meeting of shareholders at the same place at which such meeting was held. Notice need not be given of regular meetings of the Board. Any meeting may be held without notice, if all directors are present, or if notice is waived in writing, either before or after the meeting, by those not present.

Section 4. Committees. The Board of Directors may, in its discretion, by resolution passed by a majority of the whole Board, designate from among its members one or more committees which shall consist of one or more directors. The Board may designate one or more directors as alternate members of any such committee, who may replace any absent or disqualified member at

any meeting of the committee. Such committees shall have and may exercise such powers as shall be conferred or authorized by the resolution appointing them. A majority of any such committee may determine its action and fix the time and place of its meetings, unless the Board of Directors shall otherwise provide. The Board shall have power at any time to change the membership of any such committee, to fill vacancies in it, or to dissolve it.

Section 5. Action by Consent. Any action required or permitted to be taken at any meeting of the Board of Directors, or of any committee thereof, may be taken without a meeting, if prior to such action a written consent or consents thereto is signed by all members of the Board, or of such committee as the case may be, and such written consent or consents is filed with the minutes of proceedings of the Board or committee.

Section 6. Compensation. The Board of Directors may determine, from time to time, the amount of compensation which shall be paid to its members. The Board of Directors shall also have power, in its discretion, to allow a fixed sum and expenses for attendance at each regular or special meeting of the Board, or of any committee of the Board; in addition the Board of Directors shall also have power, in its discretion, to provide for and pay to directors rendering services to the Corporation not ordinarily rendered by directors, as such, special compensation appropriate to the value of such services, as determined by the Board from time to time.

Section 7. The Board of Directors from time to time may elect a Chairman of the Board. The Chairman of the Board, if one is elected, shall preside at all meetings of the Board of Directors and of the shareholders, and he shall have and perform such other duties as from time to time may be assigned to him by the Board of Directors.

ARTICLE III

OFFICERS

Section 1. Titles and Election. The officers of the Corporation, who shall be chosen by the Board of Directors at its first meeting after each annual meeting of shareholders, shall be a President, a Treasurer and a Secretary. The Board of Directors from time to time may elect one or more Vice Presidents, Assistant Secretaries, Assistant Treasurers and such other officers and agents as it shall deem necessary, and may define their powers and duties. Any number of offices may be held by the same person, except that office of President and Secretary may not be held by the same person.

Section 2. Terms of office. The officers shall hold office until their successors are chosen and qualify.

Section 3. Removal. Any officer may be removed, either with or without cause, at any time, by the affirmative vote of a majority of the Board of Directors.

Section 4. Resignations. Any officer may resign at any time giving written notice to the Board of Directors or to the Secretary. Such resignation shall take effect at the time specified therein, and, unless otherwise specified therein, the acceptance of such resignation shall not be necessary to make it effective.

Section 5. Vacancies. If the office of any officer or agent becomes vacant by reason of death, resignation, retirement, disqualification, removal from office or otherwise, the directors may choose a successor, who shall hold

office for the unexpired term in respect of which such vacancy occurred.

Section 6. President. The President shall be the chief executive officer of the Corporation and, in the absence of the Chairman, shall preside at all meetings of the Board of Directors, and of the shareholders. He shall exercise the powers and perform the duties usual to the chief executive officer and, subject to the control of the Board of Directors, shall have general management and control of the affairs and business of the Corporation; he shall appoint and discharge employees and agents of the Corporation (other than officers elected by the Board of Directors) and fix their compensation; and he shall see that all orders and resolutions of the Board of Directors are carried into effect. He shall have the power to execute bonds, mortgages and other contracts, agreements and instruments of the Corporation, and shall do and perform such other duties as from time to time may be assigned to him by the Board of Directors.

Section 7. Vice Presidents. If chosen, the Vice Presidents, in the order of their seniority, shall, in the absence or disability of the President, exercise all of the powers and duties of the President. Such Vice Presidents shall have the power to execute bonds, notes, mortgages and other contracts, agreements and instruments of the Corporation, and shall do and perform such other duties incident to the office of Vice President and as the Board of Directors or the President shall direct.

Section 8. Secretary. The Secretary shall attend all sessions of the Board and all meetings of the shareholders and record all votes and the minutes of the proceedings in a book to be kept for that purpose. He shall give, or cause to be given, notice of all meetings of the shareholders and of the Board of Directors, and shall perform such other duties as may be prescribed by the Board of Directors. The Secretary shall affix the seal of the Corporation to any instrument requiring it, and when so affixed, it shall be attested by the signature of the Secretary or an Assistant Secretary or the Treasurer or an Assistant Treasurer who may affix the seal to any such instrument in the event of the absence or disability of the Secretary. The Secretary shall have and be the

custodian of the stock records and all other books, records and papers of the Corporation (other than financial) and shall see that all books, reports, statements, certificates and other documents and records required by law are properly kept and filed.

Section 9. Treasurer. The Treasurer shall have the custody of the corporate funds and securities and shall keep full and accurate accounts of receipts and disbursements in books belonging to the Corporation and shall deposit all moneys, and other valuable effects in the name and to the credit of the Corporation, in such depositories as may be designated by the Board of Directors. He shall disburse the funds of the Corporation as may be ordered by the Board, taking proper vouchers for such disbursements, and shall render to the directors whenever they may require it, and account of all his transactions as Treasurer and of the financial condition of the Corporation.

Section 10. Duties of Officers may be Delegated. In case of the absence of disability of an officer of the Corporation, or for any other reason that the Board may deem sufficient, the Board may delegate, for the time being, the powers or duties, or any of them, of such officer to any other officer, or to any director.

ARTICLE IV

INDEMNIFICATION

Section 1. Indemnification of Directors, Officers, Employees and Agents in Actions by or in the Right of the Corporation.

(a) Subject to Section 3, the Corporation shall indemnify any person made or threatened to be made a party to an action by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that he, his testator or intestate, is or was a director, officer, employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, employee or agent of any other corporation of any type or

kind, domestic or foreign, of any partnership, joint venture, trust, employee benefit plan or other enterprise, against amounts paid in settlement and reasonable expenses, including attorneys' fees, actually and necessarily incurred by him in connection with the defense or settlement of such action, or in connection with an appeal therein, if such director, officer, employee or agent acted in good faith, for a purpose which he reasonably believed to be in, or, in the case of service for any other corporation or any partnership, joint venture, trust, employee benefit plan or other enterprise, not opposed to, the best interests of the corporation, except that no indemnification under this paragraph shall be made in respect of (1) a threatened action, or a pending action which is settled or otherwise disposed of,

or (2) any claim, issue or matter as to which such person shall have been adjudged to be liable to the Corporation, unless and only to the extent that the court in which the action was brought, or, if no action was brought, any court of competent jurisdiction, determines upon application that, in view of all the circumstances of the case, the person is fairly and reasonably entitled to indemnity for such portion of the settlement amount and expenses as the court deems proper.

Section 2. Indemnification of Directors, Officer, Employees and Agents in Other Actions or Proceedings.

(a) Subject to Section 3, the Corporation shall indemnify any person made or threatened to be made a party to an action or proceeding other than one by or in the right of the Corporation to procure a judgment in its favor, whether civil or criminal, including an action by or in the right of any other corporation of any type or kind, domestic or foreign, or any partnership, joint venture, trust, employee benefit plan or other enterprise, which any director, officer, employee or agent of the Corporation served in any capacity at the request of the Corporation, by reason of the fact that he, his testator or intestate, was a director, officer, employee or agent of the Corporation, or served such other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise in any capacity, against judgments, fines, amounts paid in settlement and reasonable expenses, including attorneys' fees actually and necessarily incurred as a result of such action or proceeding, or any appeal therein, if such director, officer, employee or agent of the Corporation acted in good faith, for a purpose which he reasonably believed to be in, or, in the case of service for any other corporation or any partnership, joint venture, trust, employee benefit plan or other enterprise, not opposed to, the best interests of the Corporation and, in criminal actions or proceedings, in addition, had no reasonable cause to believe that his conduct was unlawful.

(b) The termination of any such civil or criminal action or proceeding by judgment, settlement, conviction or upon a plea of nolo contendere, or its equivalent, shall not in itself create a presumption that any such director, officer, employee or agent of the Corporation did not act, in good faith, for a purpose which he reasonably believed to be in, or, in the case of service for any other corporation or any partnership, joint venture, trust, employee benefit plan or other enterprise, not opposed to, the best interests of the Corporation or that he had reasonable cause to believe that his conduct was unlawful.

(c) For the purpose of this Section, the Corporation shall be deemed to have requested a person to serve an employee benefit plan where the performance by such person of his duties to the Corporation also imposes duties on, or otherwise involves services by, such person to the plan or participants or beneficiaries of the plan; excise taxes assessed on a person with

respect to an employee benefit plan pursuant to applicable law shall be considered fines; and action taken or omitted by a person with respect to an employee benefit plan in the performance of such person's duties for a purpose reasonably believed by such person to be in the interest of the participants and beneficiaries of the plan shall be deemed to be for a purpose which is not opposed to the best interests of the Corporation.

Section 3. Payment of Indemnification Other Than by Court Award.

(a) A person who has been wholly successful, on the merits or otherwise, in the defense of a civil or criminal action or proceeding of the character described in Section 1 or 2 shall be entitled to indemnification as authorized in such sections.

(b) Except as provided in paragraph (a), any indemnification under Section 1 or 2, unless ordered by a court under Section 724 of the Business Corporation Law of New York, shall be made by the Corporation, only if authorized in the specific case:

(1) by the Board acting by a quorum consisting of directors who are not parties to such action or proceeding upon a finding that the director, officer, employee or agent has met the standard of conduct set forth in Section 1 or 2, as the case may be, or,

(2) if a quorum under subparagraph (1) is not obtainable or even if obtainable, a quorum of disinterested directors so directs:

(A) by the Board upon the opinion in writing of independent legal counsel that indemnification is proper in the circumstances because the applicable standard of conduct set forth in such sections has been met by such director, officer, employee or agent, or

(B) by the shareholders upon a finding that the director, officer, employee or agent has met the applicable standard of conduct set forth in such sections.

It is the policy of the Corporation that indemnification of the persons specified in Sections 1 and 2 shall be made to the fullest extent permitted by law.

(c) Expenses incurred in defending a civil or criminal action or proceeding may be paid by the Corporation in advance of the final disposition of such action or proceeding upon receipt of an undertaking by or on behalf of such director, officer, employee or agent to repay such amount as, and to the extent, required by Section 4(a).

Section 4. Other Provisions Affecting Indemnification of Directors, Officers, Employees and Agents.

(a) All expenses incurred in defending a civil or criminal action or proceeding which are advanced by the Corporation under paragraph (c) of Section 3 or allowed by a court shall be repaid in case the person receiving such advancement or allowance is ultimately found, under the procedure set forth in this Article IV or in Section 725 of the New York Business Corporation Law, not to be entitled to indemnification or, where indemnification is granted, to the extent the expenses so advance by the Corporation or allowed by the court exceed the indemnification to which he is entitled.

(b) No indemnification, advancement or allowance shall be made under this Article IV in any circumstance where it appears:

(1) that the indemnification would be inconsistent with a provision of the Certificate of Incorporation, a By-Law, a resolution of the Board of Directors or of the shareholders, an agreement or other proper corporation action, in effect at the time of the accrual of the alleged cause of action asserted in the threatened or pending action or proceeding in which the expenses were incurred or other amounts were paid, which prohibits or otherwise limits indemnification; or

(2) if there has been a settlement approved by the court, that the indemnification would be inconsistent with any condition with respect to indemnification expressly imposed by the court in approving the settlement.

(c) If, under this Article IV, any expenses or other amounts are paid by way of indemnification, otherwise than by court order or action by the shareholders, the Corporation shall, not later than the next annual meeting of shareholders unless such meeting is held within three months from the date

of such payment, and, in any event, within fifteen months from the date of such payment, mail to its shareholders of record at the time entitled to vote for the election of directors, a statement specifying the persons paid, the amounts paid and the nature and status at the time of such payment of the litigation or threatened litigation.

Section 5. Non-Exclusivity and Survival of Indemnification. The provisions of this Article IV shall not be deemed to preclude the indemnification of any person who is not specified in Section 1 or 2 but whom the Corporation has the power or obligation to indemnify under the provisions of the Business Corporation Law of New York, or otherwise. The indemnification provided by this Article IV

shall continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors, and administrators of such person. The indemnification provided by this Article IV shall not be deemed exclusive of any other rights to which directors, officers, employees or agents of the Corporation seeing indemnification or advancement of expenses may be entitled under any By-Law, agreement, contract, vote of shareholders or disinterested directors or pursuant to the direction (howsoever embodied) of any court of competent jurisdiction or otherwise, both as to actions in their official capacity and as to actions in another capacity while serving the Corporation provided that no indemnification may be made to or on behalf of any director, officer, employee or agent if a judgment or other final adjudication adverse to the officer, director, employee or agent establishes that his acts were committed in bad faith or were the result of active and deliberate dishonesty and were material to the cause of the action so adjudicated, or that he personally gained in fact a financial profit or other advantage to which he was not legally entitled.

Section 6. Insurance for Indemnification of Directors, Officers, Employees and Agents.

(a) Subject to paragraph (b) below, the Corporation shall have the power to purchase and maintain insurance:

(1) to indemnify the Corporation for any obligation which it incurs as a result of the indemnification of directors, officers, employees and agents under the provisions of this Article IV, and

(2) to indemnify directors, officers, employees and agents in instances in which they may be indemnified by the Corporation under the provisions of this Article IV, and

(3) to indemnify directors, officers, employees and agents in instances in which they may not otherwise be indemnified by the Corporation under the provisions of this Article IV provided the contract of insurance covering such directors, officers, employees and agents provides, in a manner acceptable to the superintendent of insurance, for a retention amount and for co-insurance.

(b) No insurance under paragraph (a) may provide for any payment, other than cost of defense, to or on behalf of any director, officer, employee or agent:

(1) if a judgment or other final adjudication adverse to the insured director, officer, employee or agent establishes that his acts of active and deliberate dishonesty were material to the cause of action so adjudicated, or that he personally gained in fact a financial profit or other advantage to which he was not legally entitled, or

(2) in relation to any risk the insurance of which is prohibited under the insurance law of the State of New York.

(c) Insurance under any or all subparagraphs of paragraph (a) may be included in a single contract or supplement thereto. Retrospective rated contracts are prohibited.

(d) The Corporation shall, within the time and to the persons provided in paragraph (c) of Section 4, mail a statement in respect of any insurance it has purchased or renewed under this Section, specifying the insurance carrier, date of the contract, cost of the insurance, corporate positions insured, and a statement explaining all sums, not previously reported in a statement to shareholders, paid under any indemnification insurance contract.

Section 7. Meaning of "Corporation" for Purposes of Article IV.

For purposes of this Article IV, references to "the Corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, employees or agents so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation of any type or kind, domestic or foreign, partnership, joint venture, trust, employee benefit plan or other enterprise, shall stand in the same position under the provisions of this Article IV with respect to the resulting or surviving corporation as he would have with respect to such constituent corporation if its separate existence had continued.

ARTICLE V

CAPITAL STOCK

Section 1. Certificates. The interest of each shareholder of the Corporation shall be evidenced by certificates for shares of stock in such form as the Board of Directors may from time to time prescribe. The certificates of stock shall be signed by the President or a Vice President and by the Secretary, or the Treasurer, or an Assistant Secretary, or an Assistant Treasurer, sealed with the seal of the Corporation or a facsimile thereof, and countersigned and registered in such manner, if any, as the Board of Directors may by resolution prescribe. Where any such certificate is countersigned by a transfer agent other than the Corporation or its employee, or registered by a registrar other than the Corporation or its employee, the signature of any such officer may be a facsimile signature. In case any officer or officers who shall have signed, or whose facsimile signature or signatures shall have been used on, any such certificate or certificates shall cease to be such officer or officers of the Corporation, whether

because of death, resignation or otherwise, before such certificate or certificates shall have been delivered by the Corporation, such certificate or certificates may nevertheless be adopted by the Corporation and be issued and delivered as though the person or persons who signed such certificate or certificates or whose facsimile signature or signatures shall have been used thereon had not ceased to be such officer or officers of the Corporation.

Section 2. Transfer. Subject to any restrictions or transfer of shares of stock of the Corporation of any class, series or designation contained in the Certificate of Incorporation, the shares of stock of the Corporation shall be transferred only upon the books of the Corporation by the holder thereof in person or by his attorney, upon surrender for cancellation of certificates for the same number of shares, with an assignment and power of transfer endorsed thereon or attached thereto, duly executed, with such proof of the authenticity of the signature as the Corporation or its agents may reasonably require.

Section 3. Record Dates. The Board of Directors may fix in advance a date, not less than ten nor more than sixty days preceding the date of any meeting of shareholders, or the date for the payment of any dividend, or the date for the distribution or allotment of any rights, or the date when any change, conversion or exchange of capital stock shall go into effect, as a record date for the determination of the shareholders entitled to notice of, and to vote at, any such meeting or entitled to receive payment of any such dividend, or to receive any distribution or allotment of such rights, or to exercise the rights in respect of any such change, conversion or exchange of

capital stock, and in such case only such shareholders as shall be shareholders of record on the date so fixed shall be entitled to such notice of, and to vote at, such meeting, or to receive payment of such dividend, or to receive such distribution or allotment of rights or to exercise such rights, as the case may be, notwithstanding any transfer of any stock on the books of the Corporation after any such record date fixed as aforesaid.

Section 4. Lost Certificates. In the event that any certificate of stock is lost, stolen, destroyed or mutilated, the Board of Directors may authorize the issuance of a new certificate of the same tenor and for the same number of shares in lieu thereof. The Board may in its discretion, before the issuance of such new certificate, require the owner of the lost, stolen, destroyed or mutilated certificate, or the legal representative of the owner to make an affidavit or affirmation setting forth such facts as to the loss, destruction or mutilation as it deems necessary, and to give the Corporation a bond in such reasonable sum as it directs to indemnify the Corporation.

ARTICLE VI

CHECKS, NOTES, ETC.

Section 1. Checks, Notes, Etc. All checks and drafts on the Corporation's bank accounts, and all bills of exchange and promissory notes, and all acceptances, obligations and other instruments for the payment of money, may be signed by the President or any Vice President and may also be signed by such other officer or officers, agent or agents, as shall be thereunto authorized from time to time by the Board of Directors.

ARTICLE VII

MISCELLANEOUS PROVISIONS

Section 1. Offices. The registered office of the Corporation shall be located at 777 Old Saw Mill River Road, in the City of Tarrytown, in the county of Westchester, in the State of New York, and the Corporate Secretary. The Corporation may have other offices either within or without the State of New York at such places as shall be determined from time to time by the Board of Directors or the business of the Corporation may require.

Section 2. Fiscal Year. The fiscal year of the Corporation shall be determined by the Board of Directors.

Section 3. Corporate Seal. The seal of the Corporation shall be circular in form and contain the name of the Corporation, and the year and state of its incorporation. Such seal may be altered from time to time at the discretion of the Board of Directors.

Section 4. Books. There shall be kept at such office of the Corporation as the Board of Directors shall determine, within or without the State of New York, correct books and records of account of all its business and transactions, minutes of the proceedings of its shareholders, Board of Directors and committees, and the stock book, containing the names and addresses of the shareholders, the number of shares held by them and the class or series thereof, respectively, and the dates when they respectively became the owners of record thereof, and in which the transfer of stock shall be registered, and such other books and records as the Board of Directors may from time to time determine.

Section 5. Voting of Stock. Unless otherwise specifically authorized by the Board of Directors, all stock owned by the Corporation, other

than stock of the Corporation, shall be voted, in person or by proxy, by the President or any Vice President of the Corporation on behalf of the Corporation.

Section 6. Business Advisory Board. The Corporation shall establish a Business Advisory Board which shall consist of the President of the Corporation and such other members, who may or may not be Directors, officers, or employees of the Corporation as shall be chosen by the President or the Board of Directors. The Business Advisory Board will have advisory status, and will not have the power to establish policy or procedure for the Corporation. It shall meet at least quarterly.

ARTICLE VIII

AMENDMENTS

Section 1. Amendments. These By-Laws may be amended or repealed, or new By-Laws may be adopted, by the majority of the votes cast at the meeting of shareholders by the holders of shares entitled to vote thereon. The vote of the holders of at least a majority of the voting power of the Corporation, of the shares that are issued and outstanding and entitled to vote, shall be necessary at any meeting of shareholders to amend or repeal these By-Laws or to adopt new by-laws. The By-Laws may also be amended or repealed, or new by-laws adopted, at any meeting of the Board of Directors by the vote of at least a majority of the entire Board; provided that any by-law adopted by the Board may be amended or repealed by the shareholders in the manner set forth below.

Any proposal to amend or repeal these By-Laws or to adopt new by-laws shall be stated in the notice of the meeting of the Board of Directors or the shareholders, or in the waiver of notice thereof, as the case may be, unless all of the directors or the holders of record of all of the shares of stock of the Corporation, issued and outstanding and entitled to vote, are present at such meeting.

Exhibit 10.4.1

[Merck & Co., Inc. Letterhead]

September 18, 1995
Mr. Murray Goldberg
Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, New York 10591

Dear Murray:

This shall serve to reflect our total understanding of the status of batches of INTERMEDIATE manufactured by Regeneron during a period of time following the actual manufacture of [**] batches during the CONSISTENCY and VALIDATION period but prior to the determination that such [**] batches do conform to all applicable specifications and may be released.

"All batches manufactured during the CONSISTENCY and VALIDATION period, but prior to such determination of conformity of the prior [**] batches shall be determined to have been manufactured during the first contract year notwithstanding the fact that the contract year may not commence for some period of time following their actual manufacture."

If the foregoing adequately expresses our mutual understanding, would you kindly so indicate by signing, dating and returning to us the enclosed copy of this letter agreement.

Very truly yours,

MERCK & CO., INC.

By: /s/John Pashko

THE FOREGOING IS ACCEPTED
AND REPRESENTS OUR MUTUAL
UNDERSTANDING OF THE AGREEMENT:

REGENERON PHARMACEUTICALS, INC.

By: /s/Murray Goldberg

Title: Vice President-Finance & Administration

Exhibit 10.4.2

[Merck & Co., Inc. Letterhead]

October 24, 1996

Mr. Murray Goldberg
Regeneron Pharmaceutical, Inc.
777 Old Saw Mill River road
Tarrytown, NY 10591

Dear Mr. Goldberg:

This shall serve as a memorandum of our agreement to amend Schedule A of the Manufacturing Agreement between Merck & Co., Inc. ("Merck") and Regeneron Pharmaceuticals, Inc. (Regeneron") dated September 18, 1995, so as to permit Merck to use Room [***], as depicted on the diagram annexed to Schedule A of the Manufacturing Agreement, in conjunction with Regeneron, for [***] purposes in support of the manufacture of Product pursuant to said agreement. Room [***] is indicated in red outline on the diagram attached hereto. Regeneron shall designate said area as a "[***] area" on the diagram attached to Schedule A of the Agreement.

In consideration for the [***] use of Room [***] for the term of the Agreement, Merck, within 60 days of the execution of this letter agreement by Regeneron , shall remit to Regeneron a one-time payment of [***].

If the foregoing is agreeable, would you please so indicate by signing, dating and returning to us the enclosed copy of this letter.

Very truly yours,

Merck & Co., Inc.

/s/John M. Pashko

John M. Pashko
Date: 11/25/96

The foregoing is agreed to:

Regeneron Pharmaceuticals, Inc.

/s/Murray Goldberg

Murray Goldberg
Date: 11/06/96

Exhibit 10.4.3

AMENDMENT NO. 3 TO THE MERCK-REGENERON AGREEMENT

WHEREAS, Merck & Co., Inc. and Regeneron Pharmaceuticals, Inc. entered into a Manufacturing Agreement for the INTERMEDIATE, as defined therein, effective as of September 18, 1995 (the "MANUFACTURING AGREEMENT"); and

WHEREAS, the parties amended the MANUFACTURING AGREEMENT by Letter Agreements dated September 18, 1995 and October 24, 1996; and

WHEREAS, the parties wish to further amend the MANUFACTURING AGREEMENT.

NOW, THEREFORE, the parties to the MANUFACTURING AGREEMENT do hereby agree as follows in this Amendment No. 3, entered into as of the 9th of December, 1999:

1. Section 1.7 of the MANUFACTURING AGREEMENT shall be amended by replacing Section 1.7 in its entirety with the following text which shall be incorporated into the MANUFACTURING AGREEMENT:

   "1.7 The term "CONSISTENCY AND VALIDATION PERIOD" shall mean that period of time commencing with the date of initial MANUFACTURE OF INTERMEDIATE in the FACILITY and terminating with the commencement of the first CONTRACT YEAR on November 1, 1999."

2. Section 1.8 of the MANUFACTURING AGREEMENT shall be amended by replacing Section 1.8 in its entirety with the following text which shall be incorporated into the MANUFACTURING AGREEMENT:

   "1.8 The term "CONTRACT YEAR" shall mean the period of twelve (12) consecutive calendar months commencing on the 1st day of November, 1999 and ending on the 31st day of October, 2000 and each five (5) consecutive twelve (12) month periods from November 1 through October 31 thereafter such that the second CONTRACT YEAR shall be the period from November 1, 2000 through October 31,

   2001, the third CONTRACT YEAR shall be the period from November 1, 2001 through October 31, 2002, the fourth CONTRACT YEAR shall be the period from November 1, 2002 through October 31, 2003, the fifth CONTRACT YEAR shall be the period from November 1, 2003 through October 31, 2004 and the sixth CONTRACT YEAR shall be the period from November 1, 2004 through October 31, 2005.

3. Section 13.2 (ii) shall be amended by replacing Section 13.2(ii) in its entirety with the following text which shall be incorporated into the MANUFACTURING AGREEMENT:

   "13.2(ii) A fee for each BATCH (the "BATCH FEE") of INTERMEDIATE RELEASED hereunder, as follows:

Number of BATCHES	CONTRACT YEAR 1	CONTRACT YEARS 2-4	CONTRACT YEARS 5-6
BATCHES [****]	[********]	[*******]	[********]
BATCHES [****]	[********]	[*******]	[********]
BATHCES [****]	[********]	[*******]	[********]
BATCH [**] and Over	[********]	[*******]	[********]

   No fee shall be due under this Section 13.2(ii) regarding any BATCH which is not RELEASED."

4. Section 13.2 shall be amended by adding the following text as Subsection (iii) which shall be incorporated into the MANUFACTURING AGREEMENT:

   "13.2(iii) No BATCH FEES or any other compensation will be paid by MERCK to REGENERON for any BATCH listed in Schedule X. However, if

following November 1, 1999 MERCK requests REGENERON to perform any rework of any BATCH listed in Schedule X, the parties will agree in writing on the compensation to be paid to REGENERON for the rework before it is performed."

A copy of Schedule X is attached hereto and incorporated into the MANUFACTURING AGREEMENT.

5. Section 3 of Schedule H shall be amended by replacing Section 3 in its entirety with the following text which shall be incorporated into the MANUFACTURING AGREEMENT:

"3. SHORTFALL FEE

If at the end of any CONTRACT YEAR, there are any SHORTFALL BATCHES, MERCK shall pay to REGENERON an amount ("the SHORTFALL FEE") equal To the number of SHORTFALL BATCHES in the CONTRACT YEAR multiplied by the sum of the STANDARD LABOR COST plus the BATCH FEE for that CONTRACT YEAR plus any costs, the amount of which the parties will agree to in writing on a case-by-case basis, for electricity, waste hauling, supplies and water for injection which are directly related to the fact that there are SHORTFALL BATCHES."

6. REGENERON has submitted invoices to MERCK dated December 29, 1998 ([***]) with a balance in the amount of $[***] and dated August 31, 1999 ([***]) in the amount of $[***] for activities in connection with [***] resolution. MERCK hereby agrees to pay those invoices on a non-precedent basis, making no admission that payment for activities covered by those invoices is required under the MANUFACTURING AGREEMENT. Payment of those invoices shall be made within five (5) business days of the execution date of this Amendment No. 3. MERCK's decision to make the payment is based solely on its desire to facilitate future relations between the parties. REGENRON hereby releases and forever waives any claim that it has or may have against MERCK for any and all work and activities covered by those invoices.

7. The parties have engaged in ongoing discussions concerning various issues raised by REGENERON. To resolve those discussions, MERCK hereby agrees to make the following payments to REGENERON: (a) MERCK will pay REGENERON the amount of $[***] within five (5) business days of the execution date of this Amendment No. 3 and (b) MERCK will pay REGENERON the amount of $[***] on May 1, 2000 and $[***] on each November 1 and May 1 of the second through sixth CONTRACT YEARS. However, the payment of $[***] shall only be made on such specified dates if the MANUFACTURING AGREEMENT remains in effect on the date in question, as MERCK's obligation to make any such payment ceases with the Termination of the MANUFACTURING AGREEMENT.

MERCK's decision to make the payments described in this Paragraph 7 is based solely on its desire to facilitate future Relations between the parties and is not an admission that any

such payments are required under the MANUFACTURING AGREEMENT and does not establish any precedent to that effect. In consideration of the payments and compromises set forth herein and with the intent of facilitating future relations between the parties, the sufficiency of which both parties acknowledge, MERCK and REGENERON hereby release and forever waive any claim each has or may have against the other for increases or decreases in (a) FACILITY FEE, (b) BATCH FEES or (c) any other compensation required under the MANUFACTURING AGREEMENT, except as is expressly set forth within the specific terms of the MANUFACTURING AGREEMENT, as amended, or as may otherwise be agreed to in writing by the parties.

8. Sections 1.9, 1.18 and 1.22 of the MANUFACTURING AGREEMENT shall be amended by replacing the reference in each to "Schedule A" with "Schedule A-1". Schedule A-1 is attached hereto and shall be incorporated into the MANUFACTURING AGREEMENT. However, Schedule A shall remain part of the MANUFACTURING AGREEMENT for the comparative purposes described below. MERCK understands that Schedule A-1 reflects a different and lesser space

configuration then does Schedule A. However, should the amount and type of space identified in Schedule A as [***] and [***] become necessary to MANUFACTURE INTERMEDIATE and store SUBSTANCE, MATERIAL, SUPPLIES and INTERMEDIATE, then REGENERON shall make such amount and type of space available for MERCK, as the change from Schedule A to Schedule A-1 does not in any way change or otherwise relieve REGENERON of its obligation to MERCK under Section 4.2 of the MANUFACTURING AGREEMENT.

9. Capitalized terms used in this Amendment No. 3 but not defined herein shall have the meanings as set forth in the MANUFACTURING AGREEMENT. Also, for clarity, paragraph 6 herein shall be subject to Sections 3, 24 and 25 of the MANUFACTURING AGREEMENT, paragraph 8 shall be subject to Section 4.2 of the MANUFACTURING AGREEMENT and Paragraphs 7 and 8 herein shall be subject to Sections 3, 21, 22, 24, 25, 28, 29 and 32 of the MANUFACTURING AGREEMENT.

10. This Amendment No. 3 constitutes the entire agreement among the parties on the subject matter hereof and supersedes all other prior agreements and understandings, both written or oral among the parties with respect to the subject matter of this Amendment No. 3. No modifications, changes, alterations or additions to this Amendment No. 3 shall be effective unless in writing, properly

executed by authorized representatives of both parties and identified as an amendment to this Amendment No. 3.

11. This Amendment No. 3 may be executed in one or more counterparts, each of which shall for all purposes be deemed an original and all of which shall constitute one and the same Agreement.

IN WITNESS WHEREOF, the parties hereto have executed this Amendment No. 3 as of the 9th of December 1999.

MERCK & CO., INC.	REGENERON PHARMACEUTICALS, INC.
By: /s/Bernard J. Kelley	By: /s/Murray A. Goldberg
Title: President, MMD	Title: Vice President

SCHEDULE A-1

[*****]

SCHEDULE X

[*****]

Exhibit 10.4.4

AMENDMENT NO. 4 TO THE MANUFACTURING AGREEMENT

This AMENDMENT No. 4 dated as of July 18, 2002 (the "Amendment") to the Manufacturing Agreement dated as of September 18, 1995, as amended (the "Manufacturing Agreement"), by and between Merck & Co., Inc. ("MERCK") and Regeneron Pharmaceuticals, Inc. ("REGENERON"). Capitalized terms used in this Amendment but not defined herein shall have the meaning set forth in the Manufacturing Agreement.

WHEREAS, MERCK and REGENERON have been in discussions regarding certain matters relating to the Manufacturing Agreement;

WHEREAS, both parties wish to amicably settle their differences in order to facilitate future relations between the parties;

WHEREAS, based upon the foregoing discussions, MERCK and REGENERON with to amend the Manufacturing Agreement pursuant to the terms and conditions of this Amendment;

NOW, THEREFORE, in consideration of the mutual covenants and promises herein contained, the receipt and sufficiency of which are hereby acknowledged, the parties agree to the following:

1. Over the past few months, REGENERON has raised an issue that the Manufacturing Agreement does not provide the bargained-for compensation, including profitability of the Manufacturing Agreement. MERCK disagrees with REGENERON's position and believes that REGENERON has received the bargained-for compensation. Notwithstanding the foregoing, and without agreeing upon nor acknowledging the validity of REGENERON's position, in order to resolve fully and finally the issue relating to bargained-for compensation, including, profitability of the Manufacturing Agreement, MERCK shall pay to REGENERON the amount of One Million U.S. Dollars ($1 Million) no later than thirty (30) days after the execution of this Amendment. MERCK's decision to make the payment described in this Paragraph 1 is based solely on its desire to facilitate future relations between the parties and is not an admission that any such payment is required under the Manufacturing Agreement and does not establish any precedent to that effect.

2. In consideration of the payments and compromises set forth herein and with the intent of facilitating future relations between the parties, the sufficiency of which is hereby acknowledged, REGENERON hereby releases and forever waives any claim it has or may have against MERCK relating to the bargained-for compensation, including, without limitation, the profitability of the Manufacturing Agreement or any other compensation required under the Manufacturing Agreement, except for payment of compensation as expressly set forth in Paragraph 7 or Amendment No. 3 and Article 13 and Article 19 of the Manufacturing Agreement, or as may otherwise be agreed to in writing by the parties.

3. REGENERON expressly agrees that it will abide by the terms of the Manufacturing Agreement, including, without limitation, to deliver INTERMEDIATE in accordance

with MERCK's delivery schedule, subject to the terms and conditions set forth in the Manufacturing Agreement.

4. Section 7.1 of the Manufacturing Agreement is hereby amended to add the following sentence at the end of the existing Section 7.1

"Notwithstanding anything in this Agreement to the contrary, no quarterly delivery schedule provided by MERCK in any PURCHASE ORDER shall require the delivery of more than [**] BATCHES, unless otherwise agreed in writing by the parties."

5. Section 12.3 of the Manufacturing Agreement is hereby amended to add the following sentences at the end of the existing Section 12.3;

"For purposes of determining if REGENERON has met its quarterly delivery

obligation and the BATCH FEES payable to REGENERON only, REGENERON shall be deemed to have delivered INTERMEDIATE to MERCK as of the date of receipt of the conditional release package by MERCK plus thirty (30) days (the "Deemed Delivery Date").

Notwithstanding the foregoing paragraph, in the event that MERCK has not been able to deliver MATERIALS and/or SUBSTANCE to REGENERON by the agreed-up delivery dates for such MATERIALS and/or SUBSTANCE (as agreed from time to time by MERCK and REEGENERON) or MERCK has delivered to REGENERON MATERIALS and/or SUBSTANCE which fail to meet the agreed-upon specifications then with respect to any such affected BATCHES of INTERMEDIATE, REGENERON shall not be obligated to meet MERCK's delivery schedule, but rather, shall make all reasonable effort to deliver INTERMEDIATE to MERCK as soon as possible; provided, however, that, in an such case, REGERNON shall deliver such affected BATCHES of INTERMEDIATE to MERCK no later than the CALENDAR QUARTER immediately following REGENERON's receipt of such delayed MATERIALS and/or SUBSTANCE unless the parties agree in writing to an alternate delivery schedule; provided, further, that, REGENERON shall not be obligated to deliver in any CALENDAR QUARTER more than [*****] BATCHES of INTERMEDIATE. If such affected BATCHES cannot be made up in full in the first CALENDAR QUARTER immediately following REGENERON's receipt of such delayed MATERIALS and/or SUBSTANCE due to the [*****] BATCH limitation set forth in the previous sentence, then such remaining BATCHES shall be made up in the next CALENDAR QUARTER or QUARTERS, subject to the [*****] BATCH limitation set forth in the previous sentence.

6. Section 16.2 of the Manufacturing Agreement is hereby amended to add the following sentence at the end of the existing Section 16.2;

"Notwithstanding the foregoing, in the event that MERCK gives REGENERON at least three hundred sixty five (365) days' notice of termination, then MERCK shall not be obligated to, and shall not, pay to REGENERON the aforementioned sum of [*****].

A termination notice delivered by MERCK to REGENERON pursuant to this Section 16.2 shall be non-revocable."

7. Section 13.1 of the Manufacturing Agreement shall be amended by adding an "(a)" immediately prior to the existing language and adding the following paragraphs (b), (c) and (d) immediately after the existing Section 13.1;

"(b) Notwithstanding paragraph (a) above and Section 13.2 herein, with respect to all BATCHES of INTERMEDIATE for which a [***] release package has been delivered to MERCK prior to a Resumption Date (as such term is defined in the last sentence of this paragraph (b)), REGENERON shall invoice MERCK for such BATCHES once the [***] release package has been delivered to MERCK and MERCK shall pre-pay to REGENERON [***] of the invoiced amount within forty five (45) days after the later of (i) receipt of REGENERON's invoice or (ii) the Deemed Delivery Date. The remaining [***] of the invoiced amount shall be paid by MERCK to REGERNON within thirty (30) days after the later of actual receipt by MERCK of (a) INTERMIATE or (b) REGENERON's invoice for such remaining amount. In the event that any BATCH is subsequently not RELEASED by MERCK, upon notice to REGENERON of such rejection, REGENERON shall, within thirty (30) days, either issue a credit or a check, at MERCK's option, to MERCK in the full amount pre-paid by MERCK for the rejected BATCH. No late than thirty (30) days after the start of a Prepayment Period (as such term is defined in the last sentence of this paragraph (b)), MERCK shall pay REGENERON all amounts due under this paragraph (b) relating to the BATCHES which have triggered the start of a Prepayment Period. For purposes of this Agreement, (x) "Prepayment Period" shall mean each period in which MERCK is making a prepayment pursuant to this paragraph (b) and (y) "Resumption Date" shall mean the day after the date in which MERCK has RELEASED and paid REGENERON for [***] consecutive BATCHES of INTERMEDIATE within [***] days of receipt by MERCK of the [***] release package.

(c) From and after any Resumption Date, Merck shall have no further obligation to pre-pay any amount, as provided in paragraph (b) above, and paragraph (a) above shall govern all deliveries until such time that MERCK fails to RELEASE and pay for [***] consecutive BATCHES of INTERMEDIATE within [***] days of receipt by MERCK of the applicable [***] release packages for such BATCHES, at which time a new Prepayment Period shall

commence and the terms of paragraph (b) shall again become in full force and effect until the ensuing Resumption Date.

(d) For the avoidance of any doubt, the initial Prepayment Period shall commence as of the date hereof. No later than thirty (30) days after the receipt by Merck of REGENERON's invoice, MERCK shall prepay all amounts due under paragraph (b) above for the following BATCHES: [***].

8. Schedule F shall be amended by deleting the existing Schedule F and in its place by inserting a new Schedule F, attached hereto as Attachment 1.

9. Except as specifically set forth above, all other terms and conditions of the Manufacturing Agreement shall remain unchanged and in full force and effect.

10. Each and every referenced to the Manufacturing Agreement shall hereinafter refer to the Manufacturing Agreement as amended by this Amendment.

11. This Amendment, together with the Manufacturing Agreement, are the only, entire and complete agreement of the parties relating to the subject matter hereof. All prior discussions, negotiations and agreements have been and are merged, cancelled and integrated into, and are superseded by, the Manufacturing Agreement, as amended by this Amendment. None of the parties hereto shall be bound by any conditions, definitions, warranties, understandings or representations with respect to such subject matter other than as expressly provided herein.

12. The parties acknowledge agreement to the terms of this Amendment by having an authorized representative sign one copy in the space provided below. Each party represents and warrants that the authorized representative has actual power and authority to execute this Amendment on behalf of the respective company, and that this Amendment shall be binding upon the respective company, its successors and assigns.

13. This Amendment shall be interpreted by the construed according to the substantive laws of the State of New York without reference to any rules of conflict of laws or renvoi.

14. This Amendment may be executed in one or more counterparts, each of which shall for all purposes be deemed an original and all of which shall constitute one of the same agreement.

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date first above written.

MERCK & CO., INC.	REGENERON PHARMACEUTICALS, INC.
By: /s/Bernard J. Kelley	By: /s/Murray A. Goldberg
Name: Bernard J. Kelley	Name: Murray A. Goldberg
Title: President, MMD	Title: SVP, Finance & Administration and CFO

ATTACHMENT 1

SCHEDULE F

[*****]

[RESTRICTED CONFIDENTIAL LIMITED ACCESS LOGO]

Exhibit 10.4.5

AMENDMENT NO. 5 TO THE MANUFACTURING AGREEMENT

This AMENDMENT No. 5, dated as of January 1, 2005 (this "Amendment"), to the Manufacturing Agreement dated as of September 18, 1995, as amended, (the "Manufacturing Agreement"), by and between Merck & Co., Inc. ("MERCK") and Regeneron Pharmaceuticals, Inc. ("REGENERON"). Capitalized terms used in this Amendment but not defined herein shall have the meanings set forth in the Manufacturing Agreement.

WHEREAS, MERCK and REGENERON, have been in discussions regarding certain matters relating to the extension of the term of the Manufacturing Agreement;

WHEREAS, both parties wish to extend the term of the Manufacturing Agreement and make such other changes to the Manufacturing Agreement as are set forth in this Amendment;

NOW, THEREFORE, in consideration of the mutual covenants and promises herein contained, the receipt and sufficiency of which are hereby acknowledged, the parties agree to the following:

1. Section 1.3 of the Manufacturing Agreement shall be amended by replacing Section 1.3 in its entirety with the following text:

   "1.3 The term "BATCH" shall mean one production run of INTERMEDIATE using a [******] fermenter and related purification equipment with a purification run starting with no less than [***] grams and no more than [**********]."

2. Section 1.8 of the Manufacturing Agreement shall be amended by replacing Section 1.8 in its entirety with the following text:

   "The term `CONTRACT YEAR' shall mean the period of twelve (12) consecutive calendar months commencing on the 1st day of November, 1999 and ending on the 31st day of October 2000, and each seven consecutive twelve (12) month periods from November 1 through October 31 thereafter, such that the seventh CONTRACT YEAR shall end on October 31, 2006."

3. Section 4.2 of the Manufacturing Agreement shall be amended by replacing the reference to "[******]" BATCHES of INTERMEDIATE per CONTRACT YEAR therein with a reference to "[********] BATCHES of INTERMEDIATE per CONTRACT YEAR."

4. Section 5.4 of the Manufacturing Agreement shall be amended by replacing the phrase "Upon the termination of this Agreement," in the first sentence

[RESTRICTED CONFIDENTIAL LIMITED ACCESS LOGO]

   therein with the sentence "Within thirty (30) days after the effective date of the termination of this Agreement, MERCK shall notify REGENERON in writing of its intent to remove any articles or components of the machinery and equipment identified in Schedule E and the parties shall agree on an appropriate schedule for such removal; provided, that, (i) such schedule affords MERCK a reasonable time during normal business hours to remove such articles or components and (ii) such schedule does not unnecessarily interfere with REGENERON's use of the FACILITY."

5. Section 6.1 of the Manufacturing Agreement shall be amended by replacing the third sentence therein with the following sentence:

   "The SUBSTANCE at REGENERON's FACILITY shall be stored by REGENERON in accordance with the KNOW-HOW."

6. Section 7.1 of the Manufacturing Agreement shall be amended by adding the following sentence to the end thereof:

"Notwithstanding anything in this Agreement to the contrary for CONTRACT YEAR 6, CONTRACT YEAR 7 and CONTRACT YEAR 8 (if applicable) only, no quarterly delivery schedule provided by MERCK in any PURCHASE ORDER shall require delivery of more than [******] BATCHES, and, for any full CONTRACT YEAR, the sum of the four quarterly delivery schedules provided by MERCK in the four respective PURCHASE ORDERS for that CONTRACT YEAR shall not require the delivery of more than [******] BATCHES, unless otherwise agreed in writing by the parties."

7. Section 7.2 of the Manufacturing Agreement shall be amended by replacing paragraph (a) therein in its entirety with the following text:

"(a) If both the original and revised PURCHASE ORDERS include the delivery of no more than [**] BATCHES per CONTRACT YEAR and no more than [**] BATCHES per CONTRACT QUARTER, REGENERON shall MANUFACTURE INTERMEDIATE for the balance of the CONTRACT YEAR in accordance with the revised PURCHASE ORDER."

8. Article 8 of the Manufacturing Agreement shall be amended by adding a new Section 8.12 with the following text:

"8.12 Subsequent to the execution of this Amendment, the parties shall enter into that certain Quality Agreement (the "QUALITY AGREEMENT") within three (3) months of the execution of this Amendment, which shall supplement the terms of this Article 8."

9. Section 8.3 of the Manufacturing Agreement shall be amended by replacing Section 8.3 in its entirety with the following text:

"8.3 REGENERON hereby agrees that MERCK or an AFFILIATE shall have the right to have reasonable access to the FACILITY during normal business hours in order to ascertain compliance by REGENERON with the terms of this Agreement, including but not limited to, inspection of MANUFACTURE of INTERMEDIATE, storage facilities for SUBSTANCE, MATERIALS, and SUPPLIES, all equipment and machinery used in the MANUFACTURING of INTERMEDIATE, and all records relating to such MANUFACTURE, storage facilities, equipment, and machinery. Observations and conclusions of any audit by MERCK or an Affiliate will be discussed with and then issued to REGENERON, and a written response to this audit shall be submitted to MERCK or an AFFILIATE by REGENERON within thirty (30) days after MERCK or an AFFILIATE delivers its audit report to REGENERON. Corrective action shall be agreed upon by MERCK or an AFFILIATE and REGENERON and such corrective action shall be implemented by REGENERON and MERCK within the time period agreed upon by the parties. MERCK shall have the right to request copies of all necessary documents, reports, test results, etc. evidencing completion of any such corrective action.

10. Section 8.7 of the Manufacturing Agreement shall be amended by replacing Section 8.7 in its entirety with the following text:

"8.7 Should any BATCH (i) suffer an atypical process event, as such term is described in the KNOW-HOW, (ii) be exposed to conditions which exceed environmental action limits agreed upon by MERCK and REGENERON, or (iii) otherwise fail to meet the quality control specifications, as defined in the KNOW-HOW, MERCK shall be IMMEDIATELY notified of any such circumstances upon REGENERON's discovery thereof. MERCK and REGENERON shall agree in each case on the nature and scope of any investigations to be conducted regarding such occurrence or circumstance and actions to be taken to correct any problem discovered and suitability for use relating to any BATCH involved. The final disposition, RELEASE and use of any BATCH for the generation of PRODUCT shall be at MERCK's sole discretion."

11. Section 12.3 of the Manufacturing Agreement shall be amended by replacing Section 12.3 in its entirety with the following text:

"12.3 REGENERON shall deliver the RELEASED INTERMEDIATE, which has

been packed in accordance with the KNOW-HOW, to a carrier designated by MERCK so as to allow delivery to [***], at MERCK's cost, in accordance with the mutually agreed upon delivery schedule provided by MERCK unless otherwise agreed to by the parties.

The parties agree that the delivery schedule is dependent upon multiple factors including but not limited to the supply of MATERIALS and SUBSTANCE by MERCK to REGENERON, the performance of equipment [***] to the production of INTERMEDIATE and the communication and processing of PROCESS CHANGE REQUESTS and other routine documentation; therefore the parties shall meet on a quarterly basis to review, revise and mutually agree upon the production and delivery schedules.

For purposes of determining if REGENERON has met its quarterly delivery obligation and the BATCH FEES payable to REGENERON only, REGENERON shall be deemed to have delivered INTERMEDIATE to MERCK as of the date of the receipt of the [***] plus thirty (30) days (the "Deemed Delivery Date")."

12. Section 13.1.b of the Manufacturing Agreement shall be amended by replacing the last sentence therein with the following sentence:

"For the purposes of this Agreement, (x) "Prepayment Period" shall mean each period in which MERCK is making a prepayment pursuant to this paragraph (b) and (y) "Resumption Date" shall mean the day after the date in which MERCK has RELEASED and paid REGENERON for [**] consecutive BATCHES of INTERMEDIATE within ninety (90) days of receipt by MERCK of the [***] release package."

13. Section 13.2 of the Manufacturing Agreement shall be amended by adding a new table in clause (ii) thereof following the existing table, as follows:

"Number of BATCHES	CONTRACT YEAR 7
BATCHES [***]	[$********]
BATCHES [*****]	[$********]

14. Section 13.3 of the Manufacturing Agreement shall be amended by adding clauses (iv) and (v), as follows:

(iv) The DIRECT STANDARD COST of any additional [***] run(s) required to be conducted by REGENERON (above the single run set forth in the KNOW-HOW) in order to have at least [*****] of INTERMEDIATE available to MANUFACTURE a BATCH.

(v) The cost of REGENERON's FTEs (calculated using the UNIT LABOR COST) and any out-of-pocket costs associated with AGENCY inspections of the FACILITY related to the INTERMEDIATE or its MANUFACTURE, except for costs associated with any "for cause" inspections to the extent and only to the extent arising as a result of an act or omission of REGENERON. REGENERON will invoice MERCK for such FTE costs up to a maximum of [*******] per Inspection Day (as hereinafter defined) or

up to a maximum of [*****] for each such AGENCY inspection. For the avoidance of doubt, the costs referred to in this Section 13.3(v) shall include the FTE and out-of-pocket costs required to prepare for such inspections, to respond to AGENCY observations, and related follow-up activities. As used in this Section 13.3(v), the term "Inspection Day" shall mean any calendar day on which AGENCY inspectors are present at the

FACILITY related to the INTERMEDIATE or its MANUFACTURE. If extenuating circumstances arise resulting in a prolonged AGENCY inspection of the FACILITY, the parties shall negotiate in good faith to agree on the funding of such inspection, provided, however, that nothing herein shall obligate MERCK to pay any additional costs of REGENERON relating to any such inspection.

15. Section 15.1 of the Manufacturing Agreement shall be amended by replacing Section 15.1 in its entirety with the following text:

"The initial term of this Agreement shall begin on the date first appearing above and shall continue through the termination of the seventh (7th) CONTRACT YEAR as defined herein. MERCK shall have an option to renew this AGREEMENT for one (1) additional CONTRACT YEAR exercisable with written notice to REGENERON twelve (12) months prior to the end of the seventh (7th) CONTRACT YEAR. Such renewal shall be on the same terms and conditions as set forth herein."

16. Section 16.2 of the Manufacturing Agreement shall be amended by replacing Section 16.2 in its entirety with the following text:

"MERCK shall have the right to terminate this Agreement at any time on ninety (90) days' notice prior to the date such termination shall be effective. Upon the effective date of such termination by MERCK without cause, MERCK shall pay to REGENERON the sum of [************] as liquidated damages in total satisfaction of all amounts which would otherwise thereafter become due under this Agreement. MERCK's obligation to compensate REGENERON under this Section shall not apply to the natural expiration of this Agreement or to termination of this Agreement pursuant to any other Section hereof. MERCK shall have no right to terminate this Agreement pursuant to this Section if REGENERON has properly notified MERCK under Section 16.1 that MERCK is in breach of a material provision of this Agreement, which breach remains uncured as of the date MERCK seeks to invoke the termination provisions of this Section 16.2."

17. Schedule A-1 of the Manufacturing Agreement shall be replaced with the revised and updated Schedule A-1 attached hereto.

[RESTRICTED CONFIDENTIAL LIMITED ACCESS LOGO]

18. Schedule C shall be amended by replacing the reference to "[*****************]" therein with a reference to "[****************]."

19. Schedule E shall be replaced with the revised and updated Schedule E attached hereto.

20. Schedule H shall be amended by (i) replacing the reference to "CONTRACT YEARS 5 and 6." in section 1(c) therein with a reference to "CONTRACT YEARS 5 through 7." and (ii) replacing section 2 therein in its entirety with the following text:

"2. CALCULATION OF DIRECT STANDARD COST

2(a). DIRECT STANDARD COST per BATCH shall equal the sum of STANDARD LABOR COST, STANDARD UTILITIES COST, STANDARD SUPPLIES COST and STANDARD WASTE HAULING COST, as those terms are defined in this Section, and shall be agreed to by MERCK and REGENERON at the beginning of each CONTRACT YEAR.

2(b). Components of STANDARD LABOR COST are as follows:

(i) BASE UNIT LABOR COST shall equal [**************] Dollars ($[*******]) per full time equivalent ("FTE") person.

(ii) UNIT LABOR COST in any CONTRACT YEAR shall equal BASE LABOR COST multiplied by the COST ADJUSTMENT FACTOR for that CONTRACT YEAR.

2(c). STANDARD LABOR COST shall be calculated as follows:

REGENERON and MERCK shall agree on the STANDARD LABOR COST at the beginning of each CONTRACT YEAR based on (i) the FTEs required to MANUFACTURE the number of BATCHES in the BATCH ORDER for that CONTRACT YEAR in accordance with the KNOW-HOW, (b) the UNIT LABOR COST for that CONTRACT YEAR, and (c) any adjustment needed for overtime or premium labor.

2(d). STANDARD UTILITIES COST shall equal the sum of STANDARD ELECTRICITY COST and STANDARD WFI COST.

(i) STANDARD ELECTRICITY COST in any CONTRACT YEAR shall equal BASE ELECTRICITY USAGE multiplied by UNIT ELECTRICITY COST for that CONTRACT YEAR. BASE ELECTRICITY USAGE per BATCH in kilowatt-hours shall be agreed to

by MERCK and REGENERON within thirty (30) days following the end of the CONSISTENCY AND VALIDATION PERIOD based on REGENERON's experience in MANUFACTURING INTERMEDIATE during the CONSISTENCY AND VALIDATION PERIOD. BASE ELECTRICITY USAGE shall be subject to adjustment based on actual electricity usage as measured by electricity meters in subsequent CONTRACT YEARS. UNIT ELECTRICITY COST in any CONTRACT YEAR shall equal $[***] per kilowatt-hour multiplied by the WHOLE LOT LOSS FACTOR multiplied by the COST ADJUSTMENT FACTOR for that CONTRACT YEAR.

(ii) STANDARD WFI COST in any CONTRACT YEAR shall equal BASE WFI USAGE multiplied by UNIT WFI COST for that CONTARCT YEAR. BASE WFI USAGE per BATCH in gallons shall be agreed to by MERCK and REGENERON within thirty (30) days following the end of the CONSISTENCY AND VALIDATION PERIOD based on REGENERON's experience in MANUFACTURING INTERMEDIATE during the CONSISTENCY AND VALIDATION PERIOD. UNIT WFI COST in any CONTRACT YEAR shall equal [**********] per thousand gallons multiplied by the WHOLE LOT LOSS FACTOR multiplied by the COST ADJUSTMENT FACTOR for that CONTRACT YEAR.

2(e). BASE SUPPLIES COST shall be agreed to by MERCK and REGENERON within thirty (30) days following the end of the CONSISTENCY AND VALIDATION PERIOD based on REGENERON's experience in MANUFACTURING INTERMEDIATE during the CONSISTENCY AND VALIDATION PERIOD. BASE SUPPLIES COST shall be subject to adjustment based on actual usage of SUPPLIES in subsequent CONTRACT YEARS. STANDARD SUPPLIES COST in any CONTRACT YEAR shall equal BASE SUPPLIES COSTS multiplied by the WHOLE LOT LOSS FACTOR multiplied by the COST ADJUSTMENT FACTOR for that CONTRACT YEAR.

2(f). BASE WASTE HAULING COST shall be agreed to by MERCK and REGENERON within thirty (30) days following the end of the CONSISTENCY AND VALIDATION PERIOD based on REGENERON's experience in MANUFACTURING INTERMEDIATE during the CONSISTENCY AND VALIDATION PERIOD. BASE WASTE HAULING COST shall be subject to adjustment based on actual waste quantities and associated disposal cost in subsequent CONTRACT YEARS. STANDARD WASTE HAULING COST in any CONTRACT YEAR shall equal BASE WASTE HAULING COST for that CONTRACT YEAR multiplied by the WHOLE LOT LOSS FACTOR.

[RESTRICTED CONFIDENTIAL LIMITED ACCESS LOGO]

2(g). BASE LABOR UNITS, BASE ELECTRICITY USAGE, BASE WFI USAGE, BASE SUPPLIES COST, BASE WASTE HAULING COST, and the WHOLE LOT LOSS FACTOR shall all be subject to adjustment, without maximum or minimum, at any time that the KNOW-HOW or MANUFACTURING process is changed in response to MERCK's instructions or to comply with AGENCY regulations, guidelines, or directions.

2(h). At any time that a revision is made to the PURCHASE ORDER pursuant to Section 7.2 of the Agreement:

(i) If the revision is made pursuant to Section 7.2(a), the DIRECT STANDARD COST per BATCH for the CONTRACT YEAR shall be recalculated

based on the revised BATCH ORDER. The revised DIRECT STANDARD COST shall be applied to BATCHES RELEASED thereafter. With respect to BATCHES RELEASED previously, either, as appropriate, MERCK shall PROMPTLY make an additional payment to REGENERON reflecting the increase in DIRECT STANDARD COST or REGENERON shall issue a credit to MERCK to be applied against BATCHES to be RELEASED subsequently.

(ii) If the revision is made pursuant to Section 7.2(b), REGENERON and MERCK shall agree on the STANDARD LABOR COST and DIRECT STANDARD COST to be applied to BATCHES MANUFACTURED and RELEASED in the balance of the CONTRACT YEAR in accordance with the revised PURCHASE ORDER."

2(i). DIRECT STANDARD COST to manufacture an extra [***] run (as per Section 13.3 (iv)) shall be calculated analogous to DIRECT STANDARD COST per BATCH, but shall only take into account the incremental FTE cost, UTILITIES COST, SUPPLIES COST, and WASTE HAULING COST required to manufacture such extra [***] run.

21. In consideration of Regeneron's agreement to extend the term of the Manufacturing Agreement as set forth in this Amendment, Merck hereby agrees to make payments to Regeneron in an amount equal to the EXTENSION PAYMENT on each November 1 and May 1 of the seventh and eighth CONTRACT YEARS. As used above, the term "EXTENSION PAYMENT" shall equal the product of (i) [**********] and (ii) the sum of one plus the percentage increase in the annual CPI from (a) December 31, 1999 to December 31, 2004 for the seventh CONTRACT YEAR or (b) December 31, 1999 to December 31, 2005 for the eighth CONTRACT YEAR if such CONTRACT YEAR is entered into as defined in Section 15.1. It is agreed that the EXTENSION PAYMENTS shall only be made on the dates specified in this Section 20 if the Manufacturing Agreement remains in effect

on the date in question, as Merck's obligation to make any such payment ceases with the termination of the Manufacturing Agreement. A breach of this Section 20 shall be deemed a breach of a material provision of the Manufacturing Agreement.

22. Except as specifically set forth above, all other terms and conditions of the Manufacturing Agreement shall remain unchanged and in full force and effect.

23. Each and every reference to the Manufacturing Agreement shall hereinafter refer to the Manufacturing Agreement as amended by this Amendment.

24. This Amendment, together with the Manufacturing Agreement, are the only, entire and complete agreement of the parties relating to the subject matter hereof. All prior discussions, negotiations, and agreements have been and are merged, canceled, and integrated into, and are superseded by, the Manufacturing Agreement, as amended by this Amendment. None of the parties hereto shall be bound by any conditions, definitions, warranties, understandings, or representations with respect to such subject matter other than as expressly provided herein.

25. The parties acknowledge agreement to the terms of this Amendment by having an authorized representative sign one copy in the space provided below. Each party represents and warrants that the authorized representative has actual power and authority to execute this Amendment on behalf of the respective company, and that this Amendment shall be binding upon the respective company, its successors and assigns.

26. This Amendment shall be interpreted by and construed according to the substantive laws of the State of New York without reference to any rules of conflict of laws or renvoi.

27. This Amendment may be executed in one or more counterparts, each of which shall for all purposes be deemed an original and all of which shall constitute one and the same agreement.

[RESTRICTED CONFIDENTIAL LIMITED ACCESS LOGO]

IN WITNESS WHEREOF, the parties have executed this Amendment as of the date first above written.

MERCK & CO., INC.	REGENERON PHARMACEUTICALS, INC.
By: /s/ Robert E. Dolan	By: /s/ Murray Goldberg
Name: Roberg E. Dolan	Name: Murray Goldberg
Title: VP, Vaccine & Sterile Operations	Title: VP, Finance & Administration and CFO

SCHEDULE A-1
[**********]

SCHEDULE E
[**********]

Exhibit 10.7

[Letterhead of Regeneron Pharmaceuticals, Inc.]

December 31, 1998

P. Roy Vagelos, M.D.
[* * *]
[* * *]

Dear Roy:

I am pleased to confirm Regeneron Pharmaceuticals, Inc.'s offer to employ you as a part-time employee. This letter sets forth the terms of your employment which, if acceptable, will commence effective January 1, 1999.

1. Duties. Consistent with your election by the Board of Directors of Regeneron Pharmaceuticals, Inc. (the "Company"), you will continue to serve as Chairman of the Board of Directors of the Company in accordance with our By-Laws. In addition, however, you will also provide services considerably beyond those set forth in the By-Laws that describe the duties of the Chairman of the Board. As an employee, you will attend and participate in meetings with senior management and other employees and, when appropriate, third parties, to review the operations and potential operations of the Company; assist senior management in developing operational and research strategies and plans for the Company and provide advice about implementing such strategies and plans; assist and advise in hiring and retaining senior personnel of the Company; and such other and further activities as may be reasonably required by the Company. Your activities may take place in the facilities of the Company or elsewhere, as required and reasonable. The level of effort required for these activities will approximate 30 to 50 hours per month.

2. Compensation. As an employee, you will receive an initial annual salary of $100,000. Your salary will be paid in accordance with the Company's customary payroll practices. Subject to any legal requirements or approvals, as an additional incentive, the Company will recommend to the Compensation Committee that you will be granted an option under the terms of the Company's Amended and Restated 1990 Long-Term Incentive Plan giving you the right to purchase up to 162,500 shares of the Company's Common Stock at an exercise price of the fair market value on the date of grant, with a five-year vesting schedule. In addition, the Company will annually recommend to the Compensation Committee that you be granted additional grants ("Additional Grants") on or about the first, second, third, and fourth anniversaries of the

date of grant of the option award described in the second sentence of this paragraph (the "Dates of Grant") in the amount of the greater of (a) 125,000 additional options (adjusted, as necessary, for recapitalizations or similar changes in the Company's equity structure) or (b) 125% of the highest annual grant made to an officer of the Company at the time of each respective year's annual grant to officers. Such Additional Grants are subject to compliance with legal requirements, your continued employment by the Company pursuant to this Agreement (or an amendment or amendments thereto) on the respective Date of Grant, and the existence of an appropriate option plan pursuant to which options and other awards are broadly available to employees and pursuant to which shares underlying such options or other awards have been duly authorized and are actually available for grant. You agree that the determination of the number of shares underlying the Additional Grants shall not consider extraordinary grants made to any officers (for example, as an inducement to join the Company or in connection with a promotion) and will be based on the actual grants made during the year of grant.

The Company will further recommend that the Additional Grants vest on the following schedule:

Year of Grant	Vesting
2000	4 Years

2001	3 Years
2002	2 Years
2003	1 Year

In the event of your death or disability while you are an employee of the Company, all options granted to you by the Company, whether exercisable or nonexercisable at the time of your death or disability, shall immediately become exercisable and shall immediately be subject to the terms and conditions of the appropriate option plan that govern the exercise of options by employees who die while employed by the Company (unless otherwise agreed by you and the Company).

Our Human Resources group will review with you other employment benefits for which you may be eligible.

As an employee, you will no longer be eligible to receive compensation as a member of the Board of Directors or Scientific Advisory Board, nor will you be eligible, under the current terms of Section 21 of the Company's Long-Term Incentive Plan, to receive automatic stock option grants made to nonemployee directors.

3. Proprietary Information and Confidentiality.

You understand that the Company will possess information created, discovered, or developed by, or otherwise becomes known to, the Company or in which property rights have been or may be assigned or otherwise conveyed to the Company (whether or not the information has commercial value in the business in which the

Company is or proposes to be engaged) and is treated by the Company as confidential. All such information is hereinafter called "Proprietary Information" and includes, but is not limited to, systems, processes, formulae, data, functional specifications, computer software, programs and displays, know how, improvements, discoveries, developments, designs, inventions, techniques, marketing plans, strategies, forecasts, new products, unpublished financial statements, budgets, projection, licenses, prices, costs, and customer and supplier lists, and any and all other intellectual property.

You agree that you will treat all Proprietary Information as confidential and will not, without the prior written consent of the Company, disclose or use the same other than in the course of employment. This obligation shall continue until such Proprietary Information becomes public knowledge through no fault on your part regardless of whether you continue to be employed by the Company.

4. Disclosure and Ownership of Inventions. You agree that you will promptly disclose to the Company all discoveries and inventions, whether or not patentable or registrable under copyright or similar statues, made or conceived or reduced to practice or learned by you, either alone or jointly with others, during the term of and arising out of your employment by the Company. All such discoveries and inventions are hereinafter called "Inventions". You agree that you will, at all times during the term of employment by the Company, use diligent, best efforts to avoid conflicts of interest involving potential rights and claims of the Company and of third parties to Inventions and to maximize the likelihood that any Inventions made, conceived, or developed or reduced to practice by you during the term of and arising out of your employment by the Company, will be and become the sole, unencumbered property of the Company and no other third party will have any rights thereto and that any such conflicts of interest be resolved in favor of the Company.

All Inventions shall be the sole property of the Company and its assigns, and the Company and its assigns shall be the sole owner of all patents, copyrights, trademarks, and other rights in connection therewith. You hereby assign to the Company any rights you may have or acquire in such Inventions. If the Company is unable, after reasonable effort, to secure your signature on any document or documents needed to apply for or prosecute any patent, copyright, or other right or protection relating to an Invention, for any other reason, you hereby irrevocably designate and appoint the Company and its duty authorized officers and agents as your agent and attorney-in-fact, to act for and on your behalf to execute and file any such application or applications, and to do all other lawfully permitted acts to further the prosecution and issuance of patents, copyrights, or similar protections thereon with the same legal force and effect as if executed by you, and you hereby ratify, affirm, and approve all such lawfully permitted acts accordingly.

5. Other Agreements. You represent and warrant that, to the best of your knowledge, your performance of all the terms of this Agreement does not and will not breach any agreement to keep in confidence Proprietary Information acquired by you in confidence or in trust, or any other agreement. To the best of your knowledge, you have

not entered into and shall not enter into any agreement, either written or oral, in material conflict with this Agreement.

The Company acknowledges that you serve as Chairman of the Board of Advanced Medicine Inc. and agrees that, subject to your obligations under this Agreement and as a director of the Company, you may consult for others in the future.

6. Remedies. Your covenants under this Agreement will survive termination of employment by the Company. You acknowledge that a remedy at law for any breach or threatened breach of the provisions of this Agreement would be inadequate and therefore agrees that the Company shall be entitled to injunctive relief in addition to any other available rights and remedies in case of any such breach; provided, however, that nothing contained herein shall be construed as prohibiting the Company from pursuing any other remedies available for any such breach or threatened breach.

7. EMPLOYMENT DEEMED "AT WILL". NEITHER THE EXECUTION OF THIS AGREEMENT NOR ANY TERM CONTAINED HEREIN OR IN ANY OTHER DOCUMENT, PAMPHLET, OR OTHER WRITING OR ORAL COMMUNICATION OF OR ON BEHALF OF THE COMPANY OR ANY OFFICER OR REPRESENTATIVE THEREOF SHALL BE CONSTRUED AS GIVING YOU THE RIGHT TO ANY TERM OF EMPLOYMENT WITH THE COMPANY AND THE COMPANY AND YOU AGREE THAT YOUR EMPLOYMENT MAY BE TERMINATED AT ANY TIME, WITH OR WITHOUT CAUSE, BY EITHER THE COMPANY OR YOU.

8. Governing Laws. This Agreement shall be governed by, and construed and enforced in accordance with, the laws of the State of New York.

REGENERON PHARMACEUTICALS, INC.

By: /s/Paul Lubetkin

Paul Lubetkin
Vice President, General Counsel and Secretary

AGREED AND ACCEPTED

/s/Roy Vagelos

P. Roy Vagelos, M.D.

EXHIBIT 10.15.1

FIRST AMENDMENT TO COLLABORATION AGREEMENT

This First Amendment to Collaboration Agreement (this "First Amendment") dated as of December 31, 2004, is by and between Regeneron Pharmaceuticals, Inc., a corporation organized and existing under the laws of the State of New York and having its principal office at 777 Old Saw Mill River Road, Tarrytown, New York 10591 ("Regeneron ") and Aventis Pharmaceuticals Inc., a corporation organized and existing under the laws of the State of Delaware and having a principal place of business at 200 Crossing Blvd., Bridgewater, New Jersey 08807 ("Aventis").

INTRODUCTION

WHEREAS, Regeneron and Aventis are Parties to a Collaboration Agreement, having an Effective Date of September 5, 2003 (the "Collaboration Agreement"); and

WHEREAS, Regeneron and Aventis have determined that it is desirable to amend and restate certain provisions of the Collaboration Agreement and document further agreements between them as set forth herein.

NOW, THEREFORE, in consideration of the following mutual promises and obligations and for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties, intending to be legally bound, hereby agree as follows:

Capitalized terms used in this First Amendment and not defined herein shall have the meanings ascribed to them in the Collaboration Agreement.

1. MILESTONE 1. Milestone 1 of Schedule 2 of the Collaboration Agreement is hereby amended and restated to read in its entirety as follows:

1 US $25,000,000 [**********].

2. ENTIRE AGREEMENT; SUCCESSORS AND ASSIGNS. The Collaboration Agreement, this First Amendment, and any written agreements executed by both Parties pertaining to the subject matter therein, constitute the entire agreement between the Parties hereto with respect to subject matter hereof and thereof. Said documents supersede all other agreements and understandings between the Parties with respect to the subject matter hereof and thereof, whether written or oral. This

First Amendment shall be binding upon and shall inure to the benefit of the Parties and their respective heirs, administrators, executors, Affiliates, successors and permitted assigns. Except as specifically modified by this First Amendment, all of the provisions of the Collaboration Agreement are hereby ratified and confirmed to be in full force and effect, and shall remain in full force and effect.

3. HEADINGS. The section headings contained in this First Amendment are for reference purposes only and shall not affect in any way the meaning or interpretation of the First Amendment.

4. COUNTERPARTS. This First Amendment may be executed in one or more counterparts, all of which shall be considered one and the same agreement, and shall become a binding agreement when one or more counterparts have been signed by each Party and delivered to the other Party.

5. MISCELLANEOUS. This First Amendment shall be governed by the laws of the State of New York, without regard to its principles of conflicts of laws. Each Party hereby irrevocably and unconditionally consents to the exclusive jurisdiction of the courts of the State of New York, and the United States District Court for the Southern District of New York for any action, suit or proceeding arising out of or relating to this First Amendment, waives any objections to such jurisdiction and venue and agrees not to commence any action, suit or proceeding relating to this First Amendment except in such courts. This First Amendment supersedes all prior

understandings and agreements, whether written or oral, among the Parties hereto relating to the essence of this First Amendment. If there is a direct conflict between the provisions of the Collaboration Agreement and this First Amendment, this First Amendment shall govern. This First Amendment may be amended only by a written instrument executed by each of the Parties.

[SIGNATURES APPEAR ON FOLLOWING PAGE]

IN WITNESS WHEREOF, each of the Parties has caused this First Amendment to be executed as of the date hereof by a duly authorized corporate officer.

AVENTIS PHARMACEUTICALS INC.

By: /s/ Juergen Lasowski

Name: Juergen Lasowski

Title: Vice President, Business Development & Strategy

Date: December 23, 2004

REGENERON PHARMACEUTICALS, INC.

By: /s/ Murray Goldberg

Name: Murray Goldberg

Title: SVP, Finance & Administration and CFO

Date: December 31, 2004

EXHIBIT 12.1

REGENERON PHARMACEUTICALS, INC.
COMPUTATION OF RATIO OF EARNINGS TO COMBINED FIXED CHARGES
(Dollars in thousands)

	Years ended December 31,				
	2000	2001	2002	2003	2004
Earnings:					
Income (loss) from continuing operations before income (loss) from equity investee	($ 17,077)	($ 75,178)	($124,350)	($107,395)	$ 41,565
Fixed charges	1,309	3,888	13,685	14,108	14,060
Amortization of capitalized interest	--	--	--	33	78
Interest capitalized	--	--	(222)	(276)	--
Adjusted earnings	($ 15,768)	($ 71,290)	($110,887)	($ 93,530)	$ 55,703
Fixed charges:					
Interest expense	$ 281	$ 2,657	$ 11,859	$ 11,932	$ 12,175
Interest capitalized	--	--	222	276	--
Assumed interest component of rental charges	1,028	1,231	1,604	1,900	1,885
Total fixed charges	$ 1,309	$ 3,888	$ 13,685	$ 14,108	$ 14,060
Ratio of earnings to fixed charges	(A)	(A)	(A)	(A)	3.96

(A) Due to the registrant's losses for the years ended December 31, 2000, 2001, 2002, and 2003, the ratio coverage was less than 1:1. To achieve a coverage ratio of 1:1, the registrant must generate additional earnings of the amounts shown in the table below.

	Years ended December 31,			
	2000	2001	2002	2003
Coverage deficiency	$ 17,077	$ 75,178	$ 124,572	$ 107,638

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Form S-8 (File Nos. 33-50480, 33-85330, 33-97176, 333-33891, 333-80663, 333-61132, 333-97375, and 333-119257) and on Form S-3 (File Nos. 333-74464 and 333-121225) of Regeneron Pharmaceuticals, Inc. of our report dated March 7, 2005 relating to the financial statements, management's assessment of the effectiveness of internal control over financial reporting and the effectiveness of internal control over financial reporting, which appears in this Form 10-K.

PRICEWATERHOUSECOOPERS LLP

New York, New York
March 11, 2005

Exhibit 31.1

CERTIFICATION OF CEO PURSUANT TO
RULE 13a-14(a) UNDER THE SECURITIES EXCHANGE ACT
OF 1934, AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Leonard S. Schleifer, certify that:

1. I have reviewed this annual report on Form 10-K of Regeneron Pharmaceuticals, Inc.;

2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within the registrant, particularly during the period in which this annual report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and preparation of financial statements for external purposes in accordance with generally accepted accounting principals;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this annual report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2005 By: /s/ LEONARD S. SCHLEIFER

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

Exhibit 31.2

CERTIFICATION OF CFO PURSUANT TO
RULE 13a-14(a) UNDER THE SECURITIES EXCHANGE ACT
OF 1934, AS ADOPTED PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Murray A. Goldberg, certify that:

1. I have reviewed this annual report on Form 10-K of Regeneron Pharmaceuticals, Inc.;

2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within the registrant, particularly during the period in which this annual report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and preparation of financial statements for external purposes in accordance with generally accepted accounting principals;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this annual report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officers and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 11, 2005 By: /s/ MURRAY A. GOLDBERG

Murray A. Goldberg
Senior Vice President, Finance &
Administration, Chief Financial
Officer, Treasurer, and Assistant
Secretary

EXHIBIT 32

CERTIFICATION OF CEO AND CFO PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report of Regeneron Pharmaceuticals, Inc. (the "Company") on Form 10-K for the year ended December 31, 2004 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Leonard S. Schleifer, M.D., Ph.D., as Chief Executive Officer of the Company, and Murray A. Goldberg, as Chief Financial Officer of the Company, each hereby certifies, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, to the best of his knowledge, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Leonard S. Schleifer

Leonard S. Schleifer, M.D., Ph.D.
Chief Executive Officer
March 11, 2005

/s/ Murray A. Goldberg

Murray A. Goldberg
Chief Financial Officer
March 11, 2005