REGENERON PHARMACEUTICALS INC
Form 10-K
March 12, 2007

Table of Contents

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
Form 10-K

(Mark One)

þ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2006

OR

o **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to

Commission File Number 0-19034
REGENERON PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

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

(914) 347-7000
(Registrant s telephone number, including area code)

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

None
(Title of Class)

Securities registered pursuant to Section 12(g) of the Act:
Common Stock par value $.001 per share
(Title of Class)

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes þ No o

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. Yes o No þ

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

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

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act.

Large accelerated filer o Accelerated filer þ Non-accelerated filer o

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

The aggregate market value of the common stock held by non-affiliates of the registrant was approximately $678,078,000, computed by reference to the closing sales price of the stock on NASDAQ on June 30, 2006, the last trading day of the registrant s most recently completed second fiscal quarter.

The number of shares outstanding of each of the registrant s classes of common stock as of February 28, 2007:

Class of Common Stock	Number of Shares
Class A Stock, $.001 par value	2,270,355
Common Stock, $.001 par value	63,360,389

DOCUMENTS INCORPORATED BY REFERENCE:

Specified portions of the Registrant s definitive proxy statement to be filed in connection with solicitation of proxies for its 2007 Annual Meeting of Shareholders are incorporated by reference into Part III of this Form 10-K. Exhibit index is located on pages 50 to 52 of this filing.

TABLE OF CONTENTS

Table of Contents

PART I

Item 1. *Business*

This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties relating to 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. We are currently focused on three development programs: IL-1 Trap (rilonacept) in various inflammatory indications, the VEGF Trap in oncology, and the VEGF Trap eye formulation (VEGF Trap-Eye) in eye diseases using intraocular delivery. The VEGF Trap is being developed in oncology in collaboration with the sanofi-aventis Group. In October 2006, we entered into collaboration with Bayer HealthCare LLC for the development of the VEGF-Trap-Eye. Our preclinical research programs are in the areas of oncology and angiogenesis, ophthalmology, metabolic and related diseases, muscle diseases and disorders, inflammation and immune diseases, bone and cartilage, pain, and cardiovascular diseases. We expect that our next generation of product candidates will be based on our proprietary technologies for discovering and producing human monoclonal 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.

Our core business strategy is to maintain a strong foundation in basic scientific research and discovery-enabling technology and combine that foundation with our manufacturing and clinical development capabilities to build a successful, integrated biopharmaceutical company. We believe that our ability to develop product candidates is enhanced by the application of our technology platforms. Our discovery platforms are designed to identify specific genes of therapeutic interest for a particular disease or cell type and validate targets through high-throughput production of mammalian models. Our human monoclonal antibody (VelocImmune®) and cell line expression technologies may then be utilized to design and produce new product candidates directed against the disease target. Based on the VelocImmune platform which we believe, in conjunction with our other proprietary technologies, can accelerate the development of fully human monoclonal antibodies, we plan to move two new antibody candidates into clinical trials each year going forward beginning around the end of 2007. We continue to invest in the development of enabling technologies to assist in our efforts to identify, develop, and commercialize new product candidates.

Clinical Programs:

1. IL-1 Trap Inflammatory Diseases

The IL-1 Trap (rilonacept) is a protein-based product candidate designed to bind the interleukin-1 (called IL-1) cytokine and prevent its interaction with cell surface receptors. We are evaluating the IL-1 Trap in a number of diseases and disorders in which IL-1 may play an important role, including a spectrum of rare diseases called Cryopyrin-Associated Periodic Syndromes (CAPS) and other diseases associated with inflammation.

In October 2006, we announced positive data from a Phase 3 clinical program designed to provide two separate demonstrations of efficacy for the IL-1 Trap within a single group of adult patients suffering from CAPS. The Phase 3 program of the IL-1 Trap included two studies (Part A and Part B). Both studies met their primary endpoints (Part A: $p < 0.0001$ and Part B: $p < 0.001$). The primary endpoint of both studies was the change in disease activity,

Table of Contents

which was measured using a composite symptom score composed of a daily evaluation of fever/chills, rash, fatigue, joint pain, and eye redness/pain.

We plan to submit a Biologics License Application (BLA) with the U.S. Food and Drug Administration (FDA) in the second quarter of 2007, following completion of a 24-week open-label extension phase. The FDA has granted Orphan Drug status and Fast Track designation to the IL-1 Trap for the treatment of CAPS.

The first study (Part A) was a double-blind and placebo-controlled 6-week trial, in which patients randomized to receive the IL-1 Trap had an approximate 85% reduction in their mean symptom score compared to an approximate 13% reduction in patients treated with placebo ($p<0.0001$). Following a 9-week interval during which all patients received the IL-1 Trap, a randomized withdrawal study (Part B) was performed, in which the same patients were re-randomized to either switch to placebo or continue treatment with the IL-1 Trap in a double-blind manner. During the 9-week randomized withdrawal period, patients who were switched to placebo had a five-fold increase in their mean symptom score, compared with those remaining on the IL-1 Trap who had no significant change ($p=.0002$). Both the Part A and Part B studies achieved statistical significance in all of their pre-specified secondary and exploratory endpoints.

Preliminary analysis of the safety data from both studies indicated that there were no drug-related serious adverse events. Injection site reactions and upper respiratory tract infections, all mild to moderate in nature, occurred more frequently in patients while on the IL-1 Trap than on placebo. In these two studies, the IL-1 Trap appeared to be well tolerated; 46 of 47 randomized patients completed the Part A study, and 44 of 45 randomized patients completed the Part B study. The 24-week open-label extension phase is ongoing.

CAPS is a spectrum of rare inherited inflammatory conditions, including Familial Cold Autoinflammatory Syndrome (FCAS), Muckle-Wells Syndrome (MWS), and Neonatal Onset Multisystem Inflammatory Disease (NOMID). These syndromes are characterized by spontaneous systemic inflammation and are termed autoinflammatory disorders. A novel feature of these conditions (particularly FCAS and MWS) is that exposure to mild degrees of cold temperature can provoke a major inflammatory episode that occurs within hours. CAPS are caused by a range of mutations in the gene *CIAS1* (also known as NALP3) which encodes a protein named cryopyrin (icy-fire). Currently, there are no medicines approved for the treatment of CAPS.

We are also evaluating the potential use of the IL-1 Trap in other indications in which IL-1 may play a role. Based on preclinical evidence that IL-1 appears to play a critical role in gout, we initiated a proof of concept study of the IL-1 Trap in gout in the first quarter of 2007. We are also preparing to initiate exploratory proof of concept studies of the IL-1 Trap in other indications.

Under a March 2003 collaboration agreement with Novartis Pharma AG, we retain the right to elect to collaborate in the future development and commercialization of a Novartis IL-1 antibody, which is in clinical development. Following completion of Phase 2 development and submission to us of a written report on the Novartis IL-1 antibody, we have the right, in consideration for an opt-in payment, to elect to co-develop and co-commercialize the Novartis IL-1 antibody in North America. If we elect to exercise this right, we are responsible for paying 45% of post-election North American development costs for the antibody product. In return, we are entitled to co-promote the Novartis IL-1 antibody and to receive 45% of net profits on sales of the antibody product in North America. Under certain circumstances, we are also entitled to receive royalties on sales of the Novartis IL-1 antibody in Europe.

In addition, under the collaboration agreement, Novartis has the right to elect to collaborate in the development and commercialization of a second generation IL-1 Trap following completion of its Phase 2 development, should we decide to clinically develop such a second generation product candidate. Novartis does not have any rights or options with respect to our IL-1 Trap currently in clinical development.

2. VEGF Trap Oncology

The VEGF Trap is a protein-based product candidate designed to bind all forms of Vascular Endothelial Growth Factor-A (called VEGF-A, 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-A (and to a less

Table of Contents

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.

The VEGF Trap is being developed in cancer indications in collaboration with sanofi-aventis. Currently, the collaboration is conducting Phase 2 studies, with patient enrollment underway in advanced ovarian cancer (AOC), non-small cell lung adenocarcinoma (NSCLA), and AOC patients with symptomatic malignant ascites (SMA). In 2004, the United States Food and Drug Administration (FDA) granted Fast Track designation to the VEGF Trap for the treatment of SMA. Sanofi-aventis reported in February 2007 that a registration filing is possible for the VEGF Trap in at least one of these single-agent indications in 2008.

In addition, five new Phase 2 single-agent studies have begun in conjunction with the National Cancer Institute (NCI) Cancer Therapy Evaluation Program (CTEP) in relapsed/refractory multiple myeloma, metastatic colorectal cancer, recurrent or metastatic cancer of the urothelium, locally advanced or metastatic gynecological soft tissue sarcoma, and recurrent malignant gliomas. An additional study is expected to begin shortly in metastatic breast cancer. The companies are working to finalize plans with NCI/CTEP for at least four additional trials in different cancer types.

We and sanofi-aventis intend to initiate five Phase 3 trials evaluating the safety and efficacy of the VEGF Trap in combination with standard chemotherapy regimens in specific cancer types, the first three of which are planned to begin in 2007. The companies plan to initiate these Phase 3 trials in the following indications:

first-line metastatic hormone resistant prostate cancer in combination with Taxotere®,

first-line metastatic pancreatic cancer in combination with gemcitabine-based regimen,

first-line gastric cancer in combination with Taxotere®,

second-line non-small cell lung cancer in combination with Taxotere®, and

second-line metastatic colorectal cancer in combination with FOLFIRI (Folinic Acid, Fluorouracil, and irinotecan).

Five safety and tolerability studies of the VEGF Trap in combination with standard chemotherapy regimens are continuing in a variety of cancer types to support the planned Phase 3 clinical program. The companies have previously summarized information from two of these safety and tolerability trials. One study is evaluating the VEGF Trap in combination with oxaliplatin, 5-flourouracil, and leucovorin (FOLFOX4) in a Phase 1 trial of patients with advanced solid tumors. Another study is evaluating the VEGF Trap in combination with irinotecan, 5-fluorouracil, and leucovorin (LV5FU2-CPT11) in a Phase 1 trial of patients with advanced solid tumors. Abstracts published in the 2006 ASCO Annual Meeting Proceedings reported that the VEGF Trap could be safely combined with either FOLFOX4 or LV5FU2-CPT11 at the dose levels studied. The companies are also evaluating the VEGF Trap in separate Phase 1b studies in combination with Taxotere®, cisplatin, and fluouracil; with Taxotere® and cisplatin; and with gemcitabine-erlotinib.

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 result in a cell becoming cancerous; however, a common feature of cancer cells is that they need to obtain nutrients and remove waste products, just as normal cells do. The vascular system normally supplies nutrients to and removes 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 (a process known as angiogenesis). VEGF is secreted by many tumors to stimulate the growth of new blood vessels to supply nutrients and oxygen to the tumor. VEGF blockers have been shown to inhibit new vessel growth; and, in some cases,

can cause regression of existing tumor vasculature. Countering the effects of VEGF, thereby blocking the blood supply to tumors, has demonstrated therapeutic benefits in clinical trials. This approach of inhibiting angiogenesis as a mechanism of action for an oncology medicine was 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 tumors.

Table of Contents

Collaboration with the sanofi-aventis Group

In September 2003, we entered into a collaboration agreement with Aventis Pharmaceuticals, Inc. (predecessor to sanofi-aventis U.S.) to collaborate on the development and commercialization of the VEGF Trap in all countries other than Japan, where we retained the exclusive right to develop and commercialize the VEGF Trap. 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 intraocular delivery to the eye. In December 2005, we and sanofi-aventis amended our collaboration agreement to expand the territory in which the companies are collaborating on the development of the VEGF Trap to include Japan. 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 outside of Japan for disease indications included in our collaboration. We are entitled to a royalty of approximately 35% on annual sales of the VEGF Trap in Japan, subject to certain potential adjustments. We may also receive up to $400.0 million in milestone payments upon receipt of specified marketing approvals. This total includes up to $360.0 million in milestone payments related to receipt of marketing approvals for up to eight VEGF Trap oncology and other indications in the United States or the European Union. Another $40.0 million of milestone payments relate to receipt of marketing approvals for up to five VEGF Trap oncology indications in Japan.

Under the collaboration agreement, as amended, agreed upon worldwide 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 be obligated to 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 and Japan royalties, or at a faster rate at our option.

3. VEGF Trap Eye Diseases

The VEGF Trap-Eye is a form of the VEGF Trap that has been purified and formulated with excipients and at concentrations suitable for direct injection into the eye. The VEGF Trap-Eye currently is being tested in a Phase 2 trial in patients with the neovascular form of age-related macular degeneration (wet AMD) and in a small pilot study in patients with diabetic macular edema (DME).

In the second quarter of 2006, we initiated a 150 patient, 12 week, Phase 2 trial of the VEGF Trap-Eye in wet AMD. The trial is evaluating the safety and biological effect of treatment with multiple doses of the VEGF Trap-Eye using different doses and different dosing regimens. We expect to report initial three-month data from the first 75 patients enrolled in the Phase 2 trial in early 2007 and complete three-month data on all 150 patients enrolled in the study by the end of the year. We are also conducting a Phase 1 safety and tolerability trial of a new formulation of the VEGF Trap-Eye in wet AMD. An initial Phase 3 trial of the VEGF Trap-Eye in wet AMD utilizing the new formulation is planned to begin in the second half of 2007, and a second Phase 3 trial is planned once the full data from the Phase 2 trial has been analyzed.

Also in the second quarter of 2006, we initiated a small pilot study of the VEGF Trap in patients with DME.

At the 2006 American Society of Retinal Specialists (ASRS) annual meeting in France, we updated the positive preliminary results from a Phase 1 trial of the VEGF Trap-Eye in patients with wet AMD. A total of 21 patients received a single dose of VEGF Trap-Eye at doses of 0.05, 0.15, 0.5, 1, 2, and 4 milligrams (mg) intravitreally (direct injection into the eye). Patients were evaluated for six weeks to measure the durability of effects and provide guidance for dosing regimens to be used in future trials. All dose levels were generally well tolerated, and a maximum tolerated dose was not reached in the study. In wet AMD, the leakiness of the abnormal blood vessels in the eye can lead to increased retinal thickness. On average, patients receiving the VEGF Trap-Eye demonstrated large, rapid, and

sustained (at least six weeks) reductions in retinal thickness. Excess retinal thickness, as determined by ocular coherence tomography (OCT), is a clinical measure of disease activity in wet AMD. As measured by the OCT reading center (posterior pole OCT scans), the median excess retinal thickness resulting from the disease process was 194 microns at baseline. Following a single intravitreal dose of the VEGF Trap-Eye, median excess retinal thickness was reduced to 60 microns, an improvement that was sustained over a six week period. As measured by the computerized Fast Macular Scan protocol, the median excess retinal thickness was 119 microns at baseline, which was reduced to 27 microns at six weeks after the single dose of the VEGF Trap-Eye.

Table of Contents

Of the 20 patients evaluable for efficacy, 95 percent had stabilization or improvement in visual acuity, defined as 15 letter loss on the Early Treatment of Diabetic Retinopathy Study (ETDRS) eye chart. Patients were also evaluated for best-corrected visual acuity (BCVA), the best acuity a person can achieve with glasses. BCVA for all patients in the study increased by a mean of 4.8 letters at six weeks. In the two highest dose groups (2 mg and 4 mg), the mean improvement in BCVA was 13.5 letters, with three of six patients showing an improvement in BCVA of 15 or more letters.

VEGF-A both stimulates angiogenesis and increases vascular permeability. It has been shown in preclinical studies to be a major pathogenic factor in both wet AMD and diabetic retinopathy, and it is believed to be involved in other medical problems affecting the eyes. In clinical trials, blocking VEGF-A has been shown to be effective in patients with wet AMD, and Macugen® (OSI Pharmaceuticals, Inc.) and Lucentis® (Genentech, Inc.) have been approved to treat patients with this condition.

Wet AMD and diabetic retinopathy (DR) are two of the leading causes of adult blindness in the developed world. In both conditions, severe vision loss is caused by a combination of retinal edema and neovascular proliferation. It is estimated that in the U.S. 6% of individuals aged 65-74 and 20% of those older than 75 are affected with wet 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 of the retina 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.

Collaboration with Bayer HealthCare

In October 2006, we entered into a collaboration agreement with Bayer HealthCare for the global development, and commercialization outside the United States, of the VEGF Trap-Eye. Under the agreement we and Bayer will collaborate on, and share the costs of, the development of the VEGF Trap-Eye through an integrated global plan that encompasses wet AMD, diabetic eye diseases, and other diseases and disorders. The companies will share equally in profits from any future sales of the VEGF Trap-Eye outside the United States. If the VEGF Trap-Eye is granted marketing authorization in a major market country outside the United States and the collaboration becomes profitable, we will be obligated to reimburse Bayer for 50% of the development costs that it has incurred under the agreement from our share of the collaboration profits. Within the United States, we retained exclusive commercialization rights to the VEGF Trap-Eye and are entitled to all profits from any such sales. We received an up-front payment of $75.0 million from Bayer and can earn up to $110.0 million in total development and regulatory milestones related to the development of the VEGF Trap-Eye and marketing approvals in major market countries outside the United States. We can also earn up to $135.0 million in sales milestones if total annual sales of the VEGF Trap outside the United States achieve certain specified levels starting at $200 million.

Research Technologies:

One way that a cell communicates with other cells is by releasing specific signaling proteins, either locally or into the bloodstream. These proteins have distinct functions, and are classified into different families of molecules, such as peptide hormones, growth factors, and cytokines. All of these secreted (or signaling) proteins travel to and are recognized by another set of proteins, called receptors, which reside on the surface of responding cells. These secreted proteins impact many critical cellular and biological processes, causing diverse effects ranging from the regulation of growth of particular cell types, to inflammation mediated by white blood cells. Secreted proteins can at times be overactive and thus result in a variety of diseases. In these disease settings, blocking the action of secreted proteins can have clinical benefit.

Regeneron scientists have developed two different technologies to design protein therapeutics to block the action of specific secreted proteins. The first technology, termed the Trap technology, was used to generate our current clinical pipeline, including the VEGF Trap, the VEGF Trap-Eye, and the IL-1 Trap. These novel Traps are composed of fusions between two distinct receptor components and the constant region of an antibody molecule called the Fc region , resulting in high affinity product candidates.

Table of Contents

Regeneron scientists also have discovered and developed a new technology for designing protein therapeutics that focuses on the discovery and production of fully human monoclonal antibodies. We call our technology VelocImmune® and, as described below, believe that it is a unique way of generating a wide variety of high affinity therapeutic, human monoclonal antibodies.

VelocImmune® (Human Monoclonal Antibodies)

We have developed a novel mouse technology platform, called VelocImmune, for producing fully human monoclonal antibodies. The VelocImmune mouse platform was generated by exploiting our VelociGene technology platform (see below), in a process in which six megabases of mouse immune gene loci were replaced or humanized with corresponding human immune gene loci. The VelocImmune mice can be used to generate efficiently fully human monoclonal antibodies to targets of therapeutic interest. VelocImmune and our related technologies offer the potential to increase the speed and efficiency through which human monoclonal antibody therapeutics may be discovered and validated, thereby improving the overall efficiency of our early stage drug development activities. We are utilizing the VelocImmune technology to produce our next generation of drug candidates for preclinical development and are exploring possible licensing or collaborative arrangements with third parties related to VelocImmune and related technologies.

License Agreement with AstraZeneca

In February 2007, we entered into a non-exclusive license agreement with AstraZeneca that will allow AstraZeneca to utilize our VelocImmune technology in its internal research programs to discover human monoclonal antibodies. Under the terms of the agreement, AstraZeneca made a $20.0 million non-refundable up-front payment to us. AstraZeneca also will make up to five additional annual payments of $20.0 million, subject to its ability to terminate the agreement after making the first three additional payments or earlier if the technology does not meet minimum performance criteria. We are entitled to receive a mid-single-digit royalty on any future sales of antibody products discovered by AstraZeneca using our VelocImmune technology.

VelociGene® and VelociMouse™ (Target Validation)

Our VelociGene platform allows custom and precise manipulation of very large sequences of DNA to produce highly customized alterations of a specified target gene and accelerates the production of knock-out and transgenic expression models without using either positive/negative selection or isogenic DNA. In producing knock-out models, a color or fluorescent marker is substituted in place of the actual gene sequence, allowing for high-resolution visualization of precisely where the gene is active in the body, during normal body functioning, as well as in disease processes. For the optimization of pre-clinical development and toxicology programs, VelociGene offers the opportunity to humanize targets by replacing the mouse gene with the human homolog. Thus, VelociGene allows scientists to rapidly identify the physical and biological effects of deleting or over-expressing the target gene, as well as to characterize and test potential therapeutic molecules.

The VelociMouse technology also allows for the direct and immediate generation of genetically altered mice from ES cells, thereby avoiding the lengthy process involved in generating and breeding knockout mice from chimeras. Mice generated through this method are normal and healthy and exhibit a 100% germ-line transmission frequency. Furthermore, Regeneron s VelociMice are suitable for direct phenotyping or other studies.

National Institutes of Health Grant

In September 2006, we were awarded a five-year grant from the National Institutes of Health (NIH) as part of the NIH s Knockout Mouse Project. The goal of the Knockout Mouse Project is to build a comprehensive and broadly available resource of knockout mice to accelerate the understanding of gene function and human diseases. We will use our VelociGene technology to take aim at 3,500 of the most difficult genes to target and which are not currently the focus of other large-scale knockout mouse programs. We have also agreed to grant a limited license to a consortium of research institutions, the other major participants in the Knockout Mouse Project, to use components of our VelociGene technology in the Knockout Mouse Project. We will generate a collection of targeting vectors and targeted mouse embryonic stem cells (ES cells) which can be used to produce knockout mice.

Table of Contents

These materials will be made widely available to academic researchers without charge. We will receive a fee for each targeted ES cell line or targeting construct made by us or the research consortium and transferred to commercial entities.

Under the NIH grant, we will be entitled to receive a minimum of $17.9 million over a five-year period. We will receive another $1.0 million to optimize our existing C57BL/6 ES cell line and its proprietary growth medium, both of which will be supplied to the research consortium for its use in the Knockout Mouse Project. We will have the right to use, for any purpose, all materials generated by us and the research consortium.

Cell Line Expression Technologies

Many proteins that are of potential pharmaceutical value are proteins which are secreted from the cells into the bloodstream. Examples of secreted proteins include growth factors (such as insulin and growth hormone) and antibodies. Current technologies for the isolation of cells engineered to produce high levels of secreted proteins are both laborious and time consuming. We have developed enabling platforms for the high-throughput, rapid generation of high-producing cell lines for our Traps and VelocImmune human monoclonal antibodies.

Research Programs:

Oncology and Angiogenesis

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. Vascular Endothelial Growth Factor (VEGF) was the first growth factor shown to be specific for blood vessels, by virtue of having its receptor specifically expressed on blood vessel cells. In 1994, we discovered a second family of angiogenic growth factors, termed the Angiopoietins, and we have received patents covering 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 preclinical studies have revealed that VEGF and the Angiopoietins normally function in a coordinated and collaborative manner during blood vessel growth. Manipulation of both VEGF and Angiopoietins seems to be of value in blocking vessel growth. We have research programs focusing on several targets in the areas of oncology and angiogenesis.

Tumors depend on the growth of new blood vessels (a process called angiogenesis) to support their continued growth. Therapies that block tumor angiogenesis, specifically those that block VEGF, the key initiator of tumor angiogenesis, recently have been validated in human cancer patients. However, anti-VEGF approaches do not work in all patients, and many tumors can become resistant to such therapies.

In the December 21, 2006 issue of the journal *Nature,* we reported data from a preclinical study demonstrating that blocking an important cell signaling molecule, known as Delta-like Ligand 4 (Dll4), inhibited the growth of experimental tumors by interfering with their ability to produce a functional blood supply. The inhibition of tumor growth was seen in a variety of tumor types, including those that were resistant to blockade of VEGF, suggesting a novel anti-angiogenesis therapeutic approach. A fully human monoclonal antibody to Dll4, that was discovered using our VelocImmune technology, is in preclinical development.

Metabolic and Related 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. 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 in this area encompasses the study of peripheral (hormonal) regulators of food intake and metabolism in health and disease. We have identified several targets in these therapeutic areas and are evaluating potential antibodies to evaluate in preclinical studies.

Table of Contents

Muscle Diseases and 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. We have several molecules in late stage research and are evaluating them for possible further development.

Other Therapeutic Areas

We have research programs focusing on inflammatory and immune diseases, pain, bone and cartilage, ophthalmology, and cardiovascular diseases.

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 used the facility to manufacture a product for Merck & Co., Inc. under a contract that expired in October 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, 2006, we employed 188 people at these owned and leased manufacturing facilities. There were no impairment losses associated with long-lived assets at these facilities as of December 31, 2006.

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 areas 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

We face substantial competition from pharmaceutical, biotechnology, and chemical companies (see Risk Factors *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*.). Our competitors may include Genentech, Novartis, Pfizer Inc., OSI Pharmaceuticals, Inc., Bayer HealthCare, Onyx Pharmaceuticals, Inc., Abbott Laboratories, sanofi-aventis, Merck, Amgen, Roche, 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 and VEGF Trap-Eye. 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

Table of Contents

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 method of delivery. Additionally, some of these molecules are either already approved for marketing or are at a more advanced stage of development than our product candidate.

In particular, Genentech has an approved VEGF antagonist, Avastin®, on the market for treating certain cancers and a number of pharmaceutical and biotechnology companies are working to develop competing VEGF antagonists, including Novartis, OSI Pharmaceuticals, Pfizer, and Imclone Systems Incorporated. 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 inhibitor in different cancer settings. Each of Pfizer and Onyx Pharmaceuticals (together with its partner Bayer) has received approval from the FDA to market and sell an oral medication that targets tumor cell growth and new vasculature formation that fuels the growth of tumors.

The market for eye disease products is also very competitive. Novartis and Genentech are collaborating on the commercialization and further development of a VEGF antibody fragment (Lucentis®) for the treatment of age-related macular degeneration (wet AMD) and other eye indications that was approved by the FDA in June 2006. OSI Pharmaceuticals and Pfizer are marketing an approved VEGF inhibitor (Macugen®) for wet AMD. Many other companies are working on the development of product candidates for the potential treatment of wet AMD that act by blocking VEGF, VEGF receptors, and through the use of soluble ribonucleic acids (sRNAs) that modulate gene expression. In addition, ophthalmologists are using off-label a third-party reformulated version of Genentech s approved VEGF antagonist, Avastin, with success for the treatment of wet AMD. The National Eye Institue recently has received funding for a Phase 3 trial to compare Lucentis to Avastin in the treatment of wet AMD.

IL-1 Trap. The availability of highly effective FDA approved TNF-antagonists such as Enbrel® (Amgen), Remicade® (Centocor), and Humira® (Abbott) and the IL-1 receptor antagonist Kineret (Amgen), and other marketed therapies makes it difficult to successfully develop and commercialize the IL-1 Trap. Even if the IL-1Trap 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, 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, Eli Lilly and Company and Novartis are each developing antibodies to interleukin-1 and Amgen is developing an antibody to the interleukin-1 receptor. 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.

Other Areas. Many pharmaceutical and biotechnology companies are attempting to discover new therapeutics for indications in which we invest substantial time and resources. 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 that are the focus of other research or development programs we are now conducting. These competitors include Amgen and Genentech, as well as many others. Many firms and entities are engaged in research and development in the areas of cytokines, interleukins, angiogenesis, and muscle conditions. Some of these competitors are currently conducting advanced preclinical and clinical research programs in these areas. These and other competitors may have established substantial intellectual property and other competitive advantages.

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

Table of Contents

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 these 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 (see Risk Factors *We may be restricted in our development and/or commercialization activities by, and could be subject to damage awards if we are found to have infringed, third party patents or other proprietary rights.*). 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 in an effort to develop and maintain our competitive position. We or our licensors or collaborators have filed patent applications on various products and processes relating to our product candidates 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.

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, when appropriate, 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 (see Risk Factors *If we do not obtain regulatory approval for our product candidates, we will not be able to market or sell them.*). 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 jurisdictions. 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 1, trials are conducted with a small number of subjects to determine the early safety profile of the product candidate. In Phase 2, 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 3, 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

Table of Contents

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, and other aspects of pharmaceutical 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 current and potential future local, state, federal, and foreign regulations.

Business Segments

Through 2006, our operations were managed in two business segments: research and development, and contract manufacturing. The research and development segment includes all activities related to the discovery of pharmaceutical products for the treatment of serious medical conditions, and the development and commercialization of these discoveries. It 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. The contract manufacturing segment includes all revenues and expenses related to the commercial production of products under contract manufacturing arrangements. During 2006, 2005, and 2004, the Company manufactured a product for Merck under a contract that expired in October 2006. For financial information about these segments, see Note 20, Segment Information , beginning on page F-34 in our Financial Statements. Due to the expiration of our manufacturing agreement with Merck, beginning in 2007 we only have a research and development business segment.

Employees

As of December 31, 2006, we had 573 full-time employees, of whom 80 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,

Table of Contents

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 1A. *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 described under other captions in this report 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, 2006, we had a cumulative loss of $687.6 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. Until October 31, 2006, we received contract manufacturing revenue from our agreement with Merck and, until June 30, 2005, we received contract research and development revenue from our agreement with The Procter & Gamble Company. Our agreement with Procter & Gamble expired in June 2005 and our agreement with Merck expired in October 2006. The expiration of these agreements has resulted in a significant loss of revenue to the Company.

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 early 2010, without taking into consideration the $200.0 million aggregate principal amount of convertible senior subordinated notes, which mature in October 2008; 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.

Table of Contents

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.

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 payers and on our partners ability to successfully manufacture and commercialize our product candidates. Our product candidates are delivered either by intravenous infusion or by 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.

We intend to study our lead product candidates, the VEGF Trap, VEGF Trap-Eye, and IL-1 Trap, in a wide variety of indications. We intend to study the VEGF Trap in a variety of cancer settings, the VEGF Trap-Eye in different eye diseases and ophthalmologic indications, and the IL-1 Trap in a variety of systemic inflammatory disorders. Many of these current trials are exploratory studies designed to identify what diseases and uses, if any, are best suited for our product candidates. 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 fact, our product candidates may not demonstrate the requisite efficacy and safety profile to support the continued development for any of the indications or uses.

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 or comparator drug, 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 are studying higher doses of the IL-1 Trap in different diseases after a Phase 2 trial using lower doses of the IL-1 Trap in subjects 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

Table of Contents

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 data from the Phase 3 clinical program for the IL-1 Trap in CAPS (Cryopyrin Associated Periodic Syndromes) may be inadequate to support regulatory approval for commercialization of the IL-1 Trap.

The efficacy and safety data from the Phase 3 clinical program for the IL-1 Trap in CAPS may be inadequate to support approval for its commercialization in this indication. Moreover, if the safety data from the ongoing clinical trials testing the IL-1 Trap are not satisfactory, we may not proceed with the filing of a biological license application, or BLA, for the IL-1 Trap or we may be forced to delay the filing. The FDA and other regulatory agencies may have varying interpretations of our clinical trial data, which could delay, limit, or prevent regulatory approval or clearance.

Further, before a product candidate is approved for marketing, our manufacturing facilities must be inspected by the FDA and the FDA will not approve the product for marketing if we or our third party manufacturers are not in compliance with current good manufacturing practices. Even if the FDA and similar foreign regulatory authorities do grant marketing approval for the IL-1 Trap, they may pose restrictions on the use or marketing of the product, or may require us to conduct additional post-marketing trials. These restrictions and requirements would likely result in increased expenditures and lower revenues and may restrict our ability to commercialize the IL-1 Trap profitably.

In addition to the FDA and other regulatory agency regulations in the United States, we are subject to a variety of foreign regulatory requirements governing human clinical trials, marketing and approval for drugs, and commercial sales and distribution of drugs in foreign countries. The foreign regulatory approval process includes all of the risks associated with FDA approval as well as country-specific regulations. Whether or not we obtain FDA approval for a product in the United States, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of the IL-1 Trap in those countries.

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. It is possible as we test our current drug candidates 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 our VEGF Trap-Eye candidate is being studied in 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 systemic delivery of the VEGF Trap, include bleeding, hypertension, and proteinuria. These serious side effects and other serious side effects have been reported in our systemic 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 or infusion reactions. Other VEGF blockers have reported side effects that became evident only after large scale trials or after marketing approval and large numbers of patients were treated. These include side effects that we have not yet seen in our trials such as heart attack and stroke. These and other

Table of Contents

complications or side effects could harm the development of the VEGF Trap for the treatment of cancer or the VEGF Trap-Eye for the treatment of diseases of the eye.

It is possible that safety or tolerability concerns may arise as we test higher doses of the IL-1 Trap in patients with other inflammatory diseases and disorders. Like TNF-antagonists such as Enbrel® (Amgen) and Remicade® (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 have developed hypersensitivity reactions or infusion reactions. These or other complications or side effects could impede or result in us abandoning 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 production 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 detection or appearance is often delayed, so that there can be no assurance that neutralizing antibodies will not be detected at a later date in some cases even after pivotal clinical trials have been completed. Subjects who received IL-1 Trap in clinical trials have developed antibodies. It is possible that as we test the VEGF Trap and VEGF Trap-Eye with more sensitive assays in different patient populations and larger clinical trials, we will find that subjects given the VEGF Trap and VEGF Trap-Eye produce antibodies to these product candidates, which could adversely impact the development of such candidates.

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. For example, we are currently testing a new formulation of the VEGF Trap-Eye in a Phase 1 Trial. 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, VEGF Trap-Eye, and IL-1 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.

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

Table of Contents

competitive advantages against competitors. Furthermore, even if the outcome is favorable to us, the enforcement of our intellectual property rights can be extremely expensive and time consuming.

We may be restricted in our development and/or commercialization activities by, and could be subject to damage awards if we are found to have infringed, third party patents or other proprietary rights.

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 products in clinical development, either because they claim to hold proprietary rights to the composition of a product or the way it is manufactured or used. Moreover, other parties may allege that they have blocking patents to antibody products made using our VelocImmune technology, either because of the way the antibodies are discovered or produced or because of a proprietary position covering an antibody or the antibody s target.

We are aware of patents and pending applications owned by Genentech that claim certain chimeric VEGF receptor compositions. Although we do not believe that the VEGF Trap or VEGF Trap-Eye infringes any valid claim in these patents or patent applications, Genentech could initiate a lawsuit for patent infringement and assert its patents are valid and cover the VEGF Trap or VEGF Trap-Eye. Genentech may be motivated to initiate such a lawsuit at some point in an effort to impair our ability to develop and sell the VEGF Trap or VEGF Trap-Eye, which represents a potential competitive threat to Genentech s VEGF-binding products and product candidates. An adverse determination by a court in any such potential patent litigation would likely materially harm our business by requiring us to seek a license, which may not be available, or resulting in our inability to manufacture, develop and sell the VEGF Trap or VEGF Trap-Eye or in a damage award.

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.

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 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.

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, and 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, product packagers, or labelers are unable to maintain regulatory

Table of Contents

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.

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. Any informed consent or waivers obtained from people who are enrolled in 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.

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.

Changes in the securities laws and regulations have increased, and are likely to continue to increase, our costs.

The Sarbanes-Oxley Act of 2002, which became law in July 2002, has required changes in some of our corporate governance, securities disclosure and compliance practices. Pursuant to the requirements of that Act, the SEC and the NASDAQ Stock Market have promulgated rules and listing standards covering a variety of subjects. Compliance with these new rules and listing standards has increased our legal costs, and significantly increased our accounting and auditing costs, and we expect these costs to continue. These developments may make it more difficult and more expensive for us to obtain directors and officers liability insurance. Likewise, these developments may make it more difficult for us to attract and retain qualified members of our board of directors, particularly independent directors, or qualified executive officers.

Risks Related to Our Dependence on Third Parties

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 oncology program. Sanofi-aventis funds all of the development expenses incurred by both companies in connection with the VEGF Trap oncology program. If the VEGF Trap oncology program continues, we will rely on sanofi-aventis to assist with funding the VEGF Trap program, provide commercial manufacturing capacity, enroll and monitor clinical trials, obtain regulatory approval, particularly outside the United States, and provide 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 in cancer indications will be significantly adversely affected. Sanofi-aventis has the right to terminate its collaboration agreement with us at any time upon twelve months advance notice. If sanofi-aventis were to terminate its

collaboration agreement with us, we would 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

Table of Contents

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 substantial new and additional risks to the successful development of the VEGF Trap oncology program.

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

We will rely heavily on Bayer HealthCare to assist with the development of the VEGF Trap-Eye. Under our agreement with them, Bayer HealthCare is required to fund approximately half of the development expenses incurred by both companies in connection with the global VEGF Trap-Eye development program. If the VEGF Trap-Eye program continues, we will rely on Bayer HealthCare to assist with funding the VEGF Trap-Eye development program, providing assistance with the enrollment and monitoring of clinical trials conducted outside the United States, obtaining regulatory approval outside the United States, and providing sales, marketing and commercial support for the product outside the United States. In particular, Bayer HealthCare has responsibility for selling VEGF Trap-Eye outside the United States using its sales force. While we cannot assure you that the VEGF Trap-Eye will ever be successfully developed and commercialized, if Bayer HealthCare does not perform its obligations in a timely manner, or at all, our ability to develop, manufacture, and commercialize the VEGF Trap-Eye outside the United States will be significantly adversely affected. Bayer HealthCare has the right to terminate its collaboration agreement with us at any time upon six or twelve months advance notice, depending on the circumstances giving rise to termination. If Bayer HealthCare were to terminate its collaboration agreement with us, we would not have the resources or skills to replace those of our partner, which could cause significant delays in the development and/or commercialization of the VEGF Trap-Eye outside the United States 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 outside the United States. Termination of the Bayer HealthCare collaboration agreement would create substantial new and additional risks to the successful development of the VEGF Trap-Eye development program.

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, Bayer HealthCare, 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 could experience additional costs, delays, and difficulties in the development or 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.

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

Table of Contents

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. We use our facilities to produce bulk product for clinical and preclinical candidates for ourselves and our collaborations. If our clinical candidates are discontinued, we will have to absorb one hundred percent of related 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 manufacture 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 for 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 in cancer indications, 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, including the

VEGF Trap-Eye in the United States, and we may be unsuccessful in developing our own sales, marketing, and distribution organization.

Table of Contents

Even if our product candidates are approved for marketing, their commercial success is highly uncertain because our competitors have received approval for products with the same mechanism of action, and 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.

We face substantial competition 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, Avastin® (Genentech), on the market for treating certain cancers and a number of pharmaceutical and biotechnology companies are working to develop competing VEGF antagonists, including Novartis, OSI 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 inhibitor in different cancer settings. Each of Pfizer and Onyx Pharmaceuticals (together with its partner Bayer) has received approval from the FDA to market and sell an oral medication that targets tumor cell growth and new vasculature formation that fuels the growth of tumors. The marketing approvals for Genentech s VEGF antagonist, Avastin, and their extensive, ongoing clinical development plan for Avastin in other cancer indications, 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 the FDA approved kinase inhibitors, because doctors and patients will have significant experience using these medicines. In addition, an oral medication may be considerably less expensive for patients than a biologic medication, providing a competitive advantage to companies that market such products.

The market for eye disease products is also very competitive. Novartis and Genentech are collaborating on the commercialization and further development of a VEGF antibody fragment (Lucentis®) for the treatment of age-related macular degeneration (wet AMD) and other eye indications that was approved by the FDA in June 2006. OSI Pharmaceuticals and Pfizer are marketing an approved VEGF inhibitor (Macugen®) for wet AMD. Many other companies are working on the development of product candidates for the potential treatment of wet AMD that act by blocking VEGF, VEGF receptors, and through the use of soluble ribonucleic acids (sRNAs) that modulate gene expression. In addition, ophthalmologists are using off-label a third-party reformulated version of Genentech s approved VEGF antagonist, Avastin, with success for the treatment of wet AMD. The National Eye Institute recently has received funding for a Phase 3 trial to compare Lucentis to Avastin in the treatment of wet AMD. The marketing approval of Macugen and Lucentis and the potential off-label use of Avastin make it more difficult for us to enroll patients in our clinical trials and successfully develop the VEGF Trap-Eye. Even if the VEGF Trap-Eye is ever approved for sale for the treatment of eye diseases, it may be difficult for our drug to compete against Lucentis or Macugen, because doctors and patients will have significant experience using these medicines. Moreover, the relatively low cost of therapy with Avastin in patients with wet AMD presents a further competitive challenge in this indication.

The availability of highly effective FDA approved TNF-antagonists such as Enbrel® (Amgen), Remicade® (Centocor), and Humira® (Abbott Laboratories), and the IL-1 receptor antagonist Kineret® (Amgen), and other marketed therapies, makes it more difficult to successfully develop and commercialize the IL-1 Trap. This is one of the reasons we discontinued the development of the IL-1 Trap in adult rheumatoid arthritis. 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 in indications where both are useful because doctors and patients will have significant experience using these effective medicines. Moreover, in such indications these approved therapeutics may offer competitive advantages over the IL-1 Trap, such as requiring fewer injections.

Table of Contents

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, Eli Lilly and Company and Novartis are each developing antibodies to interleukin-1 and Amgen is developing an antibody to the interleukin-1 receptor. 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. For example, we may find it difficult to enroll patients in clinical trials for the IL-1 Trap if the companies developing these competing interleukin-1 inhibitors commence clinical trials in the same indications.

We are developing the IL-1 Trap for the treatment of a spectrum of rare diseases associated with mutations in the *CIAS*1 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 payers and these payers may not agree to cover or reimburse for use of our products.

Our products, if commercialized, may be significantly more expensive than traditional drug treatments. Our future revenues and profitability will be adversely affected if United States and foreign governmental, private third-party insurers and payers, and other third-party payers, including Medicare and Medicaid, do not agree to defray or reimburse the cost of our products to the patients. If these entities refuse to provide coverage and reimbursement with respect to our products or provide an insufficient level of coverage and reimbursement, our products may be too costly for many patients to afford them, and physicians may not prescribe them. Many third-party payers cover only selected drugs, making drugs that are not preferred by such payer more expensive for patients, and require prior authorization or failure on another type of treatment before covering a particular drug. Payers may especially impose these obstacles to coverage on higher-priced drugs, as our product candidates are likely to be.

We intend to file an application with the FDA seeking approval to market the IL-1 Trap for the treatment of a spectrum of rare genetic disorders called CAPS. There may be too few patients with CAPS to profitably commercialize the IL-1 Trap. Physicians may not prescribe the IL-1 Trap and CAPS patients may not be able to afford the IL-1 Trap if third party payers do not agree to reimburse the cost of IL-1 Trap therapy and this would adversely affect our ability to commercialize the IL-1 Trap profitably.

In addition to potential restrictions on coverage, the amount of reimbursement for our products may also reduce our profitability. In the United States, there have been, and we expect will continue to be, actions and proposals to control and reduce healthcare costs. Government and other third-party payers are challenging the prices charged for healthcare products and increasingly limiting, and attempting to limit, both coverage and level of reimbursement for prescription drugs.

Since our products, including the IL-1 Trap, will likely be too expensive for most patients to afford without health insurance coverage, if our products are unable to obtain adequate coverage and reimbursement by third-party payers our ability to successfully commercialize our product candidates may be adversely impacted. Any limitation on the use of our products or any decrease in the price of our products will have a material adverse effect on our ability to achieve profitability.

In certain foreign countries, pricing, coverage and level of reimbursement of prescription drugs are subject to governmental control, and we may be unable to negotiate coverage, pricing, and reimbursement on terms that are favorable to us. In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully

marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. Our results of operations may suffer if we are unable to market our products in foreign countries or if coverage and reimbursement for our products in foreign countries is limited.

Table of Contents

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 certain of 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 P. Roy Vagelos, M.D., the Chairman of our board of directors, Leonard Schleifer, M.D., Ph.D., our President and Chief Executive Officer, George D. Yancopoulos, M.D., Ph.D., our Executive Vice President, Chief Scientific Officer and President, Regeneron Research Laboratories, and Neil Stahl, Ph.D., our Senior Vice President, Research and Development Sciences. 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 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.

In future years, if we or our independent registered public accounting firm are unable to conclude that our internal control over financial reporting is effective, the market value of our common stock could be adversely affected.

As directed by Section 404 of the Sarbanes-Oxley Act of 2002, the SEC adopted rules requiring public companies to include a report of management on the Company s internal control over financial reporting in their annual reports on Form 10-K that contains an assessment by management of the effectiveness of our internal control over financial reporting. In addition, the independent registered public accounting firm auditing our financial statements must attest to and report on management s assessment and on the effectiveness of our internal control over financial reporting. Our independent registered public accounting firm provided us with an unqualified report as to our assessment and the effectiveness of our internal control over financial reporting as of December 31, 2006, which report is included in this Annual Report on Form 10-K. However, we cannot assure you that management or our independent registered public accounting firm will be able to provide such an assessment or unqualified report as of future year-ends. In this event, investors could lose confidence in the reliability of our financial statements, which could result in a decrease in the market value of our common stock.

Table of Contents

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 December 31, 2006, our seven largest shareholders, including sanofi-aventis, beneficially owned 41.1% of our outstanding shares of Common Stock, assuming, in the case of Leonard S. Schleifer, M.D. Ph.D., our Chief Executive Officer, and P. Roy Vagelos, M.D., our Chairman, the conversion of their Class A Stock into Common Stock and the exercise of all options held by them which are exercisable within 60 days of December 31, 2006. As of December 31, 2006, sanofi-aventis owned 2,799,552 shares of Common Stock, representing 4.4% of the shares of Common Stock then outstanding. Under our stock purchase agreement with sanofi-aventis, sanofi-aventis may sell no more than 500,000 of these shares in any calendar quarter. If 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, 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 generally 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 December 31, 2006, holders of Class A Stock held 26.5% of the combined voting power of all of Common Stock and Class A Stock then outstanding. 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 December 31, 2006:

- our current officers and directors beneficially owned 13.3% of our outstanding shares of Common Stock, assuming conversion of their Class A Stock into Common Stock and the exercise of all options held by such persons which are exercisable within 60 days of December 31, 2006, and 30.5% of the combined voting power of our outstanding 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 December 31, 2006; and

- our seven largest shareholders beneficially owned 41.1% of our outstanding shares of Common Stock assuming, in the case of Leonard S. Schleifer, M.D., Ph.D., our Chief Executive Officer, and P. Roy Vagelos, M.D., our Chairman, the conversion of their Class A Stock into Common Stock and the exercise of all options held by them which are exercisable within 60 days of December 31, 2006. In addition, these seven shareholders held 48.7% of the combined voting power of our outstanding shares of Common Stock and Class A Stock, assuming the exercise of all options held by our Chief Executive Officer and our Chairman which are exercisable within 60 days of December 31, 2006.

The anti-takeover effects of provisions of our charter, by-laws, 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 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;

Table of Contents

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 two-thirds 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.*

In addition, we have a Change in Control Severance Plan and our chief executive officer has an employment agreement that provides severance benefits in the event our officers are terminated as a result of a change in control of the Company. 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 our company, as defined in the plan.

Item 1B. ***Unresolved Staff Comments***

None.

Item 2. ***Properties***

We conduct our research, development, manufacturing, and administrative activities at our owned and leased facilities. We currently lease approximately 236,000 square feet of laboratory and office space in Tarrytown, New York.

In December 2006, we entered into a new operating lease agreement for approximately 221,000 square feet of laboratory and office space at our current Tarrytown location. The new lease includes approximately 27,000 square feet that we currently occupy (our retained facilities) and approximately 194,000 square feet to be located in new facilities that will be constructed and which are expected to be completed in early-2009. The term of the lease is expected to commence in early-2008 and will expire approximately 16 years later. Under the new lease we also have various options and rights on additional space at the Tarrytown site, and will continue to lease our present facilities until the new facilities are ready for occupancy. In addition, the lease contains three renewal options to extend the term of the lease by five years each and early termination options for our retained facilities only. The lease provides for monthly payments over the term of the lease related to our retained facilities, the costs of construction and tenant improvements for our new facilities, and additional charges for utilities, taxes, and operating expenses.

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 (2)	209,000	March, 2009 (3)	$ 309,000	none
Tarrytown (2)	194,000	March, 2024 (3)		three 5-year terms
Tarrytown	27,000	March, 2024 (3)	$ 52,000	three 5-year terms
Rensselaer	75,000	July 11, 2012	$ 25,000	one 5-year term

Table of Contents

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

(2) Upon completion of the new facilities, as described above, we will release the 209,000 square feet of space in our current facility and take over 194,000 square feet in the newly constructed buildings.

(3) Estimated based upon expected completion of our new facilities, as described above.

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***

From time to time, we are a party to legal proceedings in the course of our business. We do not expect any such current 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***

No matters were submitted to a vote of our security holders during the last quarter of the fiscal year ended December 31, 2006.

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
2005		
First Quarter	$ 9.36	$ 4.75
Second Quarter	8.84	4.61
Third Quarter	10.67	7.36
Fourth Quarter	17.37	8.55
2006		
First Quarter	$ 18.00	$ 14.35
Second Quarter	16.69	10.97
Third Quarter	17.00	10.88
Fourth Quarter	24.85	15.27

As of February 28, 2007, there were 538 shareholders of record of our Common Stock and 44 shareholders of record of our Class A Stock.

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 2007 Annual Meeting of Shareholders to be filed with the SEC is incorporated by reference into Item 12 of this Report on Form 10-K.

Table of Contents

STOCK PERFORMANCE GRAPH

Set forth below is a line graph comparing the cumulative total shareholder return on Regeneron s Common Stock with the cumulative total return of (i) The NASDAQ Pharmaceuticals Stocks Index and (ii) The NASDAQ Stock Market (U.S.) Index for the period from December 31, 2001 through December 31, 2006. The comparison assumes that $100 was invested on December 31, 2001 in our Common Stock and in each of the foregoing indices. All values assume reinvestment of the pre-tax value of dividends paid by companies included in these indices. The historical stock price performance of our Common Stock shown in the graph below is not necessarily indicative of future stock price performance.

	12/31/2001	12/31/2002	12/31/2003	12/31/2004	12/31/2005	12/31/2006
Regeneron	$ 100.00	$ 65.73	$ 52.24	$ 32.71	$ 56.46	$ 71.27
NASDAQ Pharm	100.00	64.62	94.72	100.88	111.09	108.75
NASDAQ US	100.00	69.13	103.36	112.49	114.88	126.22

Table of Contents

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

The selected financial data set forth below for the years ended December 31, 2006, 2005, and 2004 and at December 31, 2006 and 2005 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, 2003 and 2002 and at December 31, 2004, 2003, and 2002 are derived from our audited financial statements not included in this report.

	Year Ended December 31,				
	2006	2005	2004	2003	2002
	(In thousands, except per share data)				
Statement of Operations Data					
Revenues					
Contract research and development	$ 51,136	$ 52,447	$ 113,157	$ 47,366	$ 10,924
Research progress payments			42,770		
Contract manufacturing	12,311	13,746	18,090	10,131	11,064
	63,447	66,193	174,017	57,497	21,988
Expenses					
Research and development	137,064	155,581	136,095	136,024	124,953
Contract manufacturing	8,146	9,557	15,214	6,676	6,483
General and administrative	25,892	25,476	17,062	14,785	12,532
	171,102	190,614	168,371	157,485	143,968
Income (loss) from operations	(107,655)	(124,421)	5,646	(99,988)	(121,980)
Other income (expense)					
Other contract income		30,640	42,750		
Investment income	16,548	10,381	5,478	4,462	9,462
Interest expense	(12,043)	(12,046)	(12,175)	(11,932)	(11,859)
	4,505	28,975	36,053	(7,470)	(2,397)
Net income (loss) before cumulative effect of a change in accounting principle	(103,150)	(95,446)	41,699	(107,458)	(124,377)
Cumulative effect of adopting Statement of Accounting Standards No. 123R (SFAS 123R)	813				
Net income (loss)	$ (102,337)	$ (95,446)	$ 41,699	$ (107,458)	$ (124,377)
Net income (loss) per share, basic:	$ (1.78)	$ (1.71)	$ 0.75	$ (2.13)	$ (2.83)

Net income (loss) before cumulative effect of a change in accounting principle					
Cumulative effect of adopting SFAS 123R	0.01				
Net income (loss)	$ (1.77)	$ (1.71)	$ 0.75	$ (2.13)	$ (2.83)
Net income (loss) per share, diluted	$ (1.77)	$ (1.71)	$ 0.74	$ (2.13)	$ (2.83)

Table of Contents

	At December 31,				
	2006	2005	2004	2003	2002
			(In thousands)		
Balance Sheet Data					
Cash, cash equivalents, marketable securities, and restricted marketable securities (current and non-current)	$ 522,859	$ 316,654	$ 348,912	$ 366,566	$ 295,246
Total assets	585,090	423,501	473,108	479,555	391,574
Notes payable long-term portion	200,000	200,000	200,000	200,000	200,000
Stockholders equity	216,624	114,002	182,543	137,643	145,981

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 focused on three development programs: IL-1 Trap (rilonacept) in various inflammatory indications, the VEGF Trap in oncology, and the VEGF Trap-Eye formulation in eye diseases using intraocular delivery. The VEGF Trap is being developed in oncology in collaboration with the sanofi-aventis Group. In October 2006, we entered into collaboration with Bayer HealthCare LLC for the development of the VEGF Trap-Eye. Our preclinical research programs are in the areas of oncology and angiogenesis, ophthalmology, metabolic and related diseases, muscle diseases and disorders, inflammation and immune diseases, bone and cartilage, pain, and cardiovascular diseases. We expect that our next generation of product candidates will be based on our proprietary technologies for developing human monoclonal 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 we 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, 2006, we had a cumulative loss of $687.6 million. In the absence of revenues from the commercialization of our product candidates or other sources, the amount, timing, nature, and 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-Eye and IL-1 Trap; advance new product candidates into clinical development from our existing research programs utilizing our new technology for designing fully human monoclonal antibodies; continue our research and development programs; and commercialize product candidates that receive regulatory approval, if any. Also, our activities may expand over time and 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 be profitable 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 2006, our research and development expenses totaled $137.1 million. We expect these expenses to increase substantially in 2007 as we begin Phase 3 clinical trials of the VEGF Trap-Eye, expand our IL-1 Trap clinical program, advance our antibody development program, and increase our research and development headcount. 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, and payments for our research and development activities.

Table of Contents

A primary driver of our expenses is our number of full-time employees. Our annual average headcount in 2006 was 573 compared with 696 in 2005 and 721 in 2004. In 2006, our average annual headcount decreased primarily as a result of reductions made in the fourth quarter of 2005 and mid-year in 2006. These workforce reductions were associated with narrowing the focus of our research and development efforts, substantial improvements in manufacturing productivity, the June 2005 expiration of our collaboration with Procter & Gamble, and the completion of contract manufacturing for Merck in October 2006. In 2007, we expect our annual average headcount to increase to approximately 650 due, in part, to our expanded development programs for the VEGF Trap-Eye and IL-1 Trap, and our plans to move two new antibody candidates into clinical trials every year beginning around the end of 2007.

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 2006 and plans for 2007 are as follows:

Product Candidate		2006 Events	2007 Events/Plans
VEGF Trap	Oncology	Initiated Phase 2 studies of the VEGF Trap as a single agent in AOC and NSCLA patients, and in AOC patients with SMA. Initiated two safety and tolerability studies of the VEGF Trap in combination with standard chemotherapy regimens Reported preliminary results of the safety and tolerability of intravenous VEGF Trap plus FOLFOX4 and of intravenous VEGF Trap plus LV5FU2-CPT11 in separate Phase 1 trials of patients with advanced solid tumors	Sanofi-aventis to initiate at least three of five Phase 3 studies of the VEGF Trap in combination with standard chemotherapy regimens in specific cancer indications NCI/CTEP initiated five Phase 2 studies of the VEGF Trap as a single agent in relapsed/refractory multiple myeloma, metastatic colorectal cancer, recurrent or metastatic cancer of the urothelium, locally advanced or metastatic gynecological soft tissue sarcoma, and recurrent malignant gliomas NCI/CTEP finalized protocol for Phase 2 trial of the VEGF Trap as a single agent in metastatic breast cancer NCI/CTEP to initiate at least four new exploratory efficacy/safety studies evaluating the VEGF Trap in a variety of cancer types
VEGF Trap	Eye	Reported positive preliminary results from Phase 1 trial in wet AMD utilizing intravitreal injections in 21 patients up to a top dose of 4 mg Initiated Phase 2 trial in wet AMD utilizing intravitreal injections	Report interim results of Phase 2 trial in wet AMD utilizing intravitreal injections Initiate first Phase 3 trial in wet AMD utilizing intravitreal injections of the VEGF Trap-Eye compared with Lucentis® Report final results of Phase 2 trial in wet AMD utilizing intravitreal injections

Initiated safety and tolerability study of a new formulation of the VEGF Trap-Eye in patients with wet AMD	Report results of the Phase 1 trial in DME
Initiated Phase 1 trial in DME	Explore additional eye disease indications
Initiated collaboration with Bayer HealthCare	

Table of Contents

Product Candidate	2006 Events	2007 Events/Plans
IL-1 Trap (rilonacept)	Reported positive results from efficacy portion of Phase 3 trial of the IL-1 Trap in CAPS Reported preliminary results from ongoing Phase 1 trial in SJIA	Submit Biologics License Application (BLA) with the FDA for CAPS Initiate proof-of-concept studies evaluating the IL-1 Trap in gout and report initial data Evaluate the IL-1 Trap in other disease indications in which IL-1 may play an important role
VelocImmune	Discovered multiple antibodies against more than ten different therapeutic targets	Finalize plans to initiate clinical trials of two antibodies against different therapeutic targets Advance two new antibodies into preclinical development

Collaborations

Our current collaboration agreements with sanofi-aventis, Bayer, and Novartis Pharma AG, and our expired agreement with The Procter & Gamble Company are summarized below.

The sanofi-aventis Group

In September 2003, we entered into a collaboration agreement with Aventis Pharmaceuticals Inc. (now a member of the sanofi-aventis Group) to collaborate on the development and commercialization of the VEGF Trap in all countries other than Japan, where we retained the exclusive right to develop and commercialize 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 intraocular delivery to the eye. In connection with this amendment, sanofi-aventis made a $25.0 million non-refundable payment to us.

In December 2005, we and sanofi-aventis amended our collaboration agreement to expand the territory in which the companies are collaborating on the development of the VEGF Trap to include Japan. In connection with this amendment, sanofi-aventis agreed to make a $25.0 million non-refundable up-front payment to us, which was received in January 2006. 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 outside of Japan, for disease indications included in our collaboration. We are entitled to a royalty of approximately 35% on annual sales of the VEGF Trap in Japan, subject to certain potential adjustments. We may also receive up to $400.0 million in milestone payments upon receipt of specified marketing approvals. This total includes up to $360.0 million in milestone payments related to the receipt

of marketing approvals for up to eight VEGF Trap oncology and other indications in the United States or the European Union. Another $40.0 million of milestone payments relate to receipt of marketing approvals for up to five VEGF Trap oncology indications in Japan. 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.

Regeneron has agreed 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 worldwide 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 be obligated to 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

Table of Contents

collaboration profits and Japan royalties, or at a faster rate at our option. Since inception of the collaboration through December 31, 2006, we and sanofi-aventis have incurred $205.0 million in agreed upon development expenses related to VEGF Trap program. In addition, if the first commercial sale of a VEGF Trap product for intraocular delivery to the eye 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.

Bayer Healthcare LLC

In October 2006, we entered into a license and collaboration agreement with Bayer to globally develop, and commercialize outside the United States, the VEGF Trap-Eye. Under the terms of the agreement, Bayer made a non-refundable up-front payment to us of $75.0 million. In addition, we are eligible to receive up to $110.0 million in development and regulatory milestones, including a total of $40.0 million upon the initiation of Phase 3 trials in defined major indications such as wet AMD and DME. We are also eligible to receive up to an additional $135.0 million in sales milestones when and if total annual sales of the VEGF Trap-Eye outside the United States achieve certain specified levels starting at $200.0 million.

We will share equally with Bayer in any future profits arising from the commercialization of the VEGF Trap-Eye outside the United States. If the VEGF Trap-Eye is granted marketing authorization in a major market country outside the United States and the collaboration becomes profitable, we will be obligated to reimburse Bayer out of our share of the collaboration profits for 50% of the agreed upon development expenses that Bayer has incurred in accordance with a formula based on the amount of development expenses that Bayer has incurred and our share of the collaboration profits, or at a faster rate at our option. Within the United States, we are responsible for any future commercialization of the VEGF Trap-Eye and have retained exclusive rights to any future profits arising therefrom.

Agreed upon development expenses incurred by both companies, beginning in 2007, under a global development plan will be shared as follows:

2007: Up to $50.0 million shared equally; we are solely responsible for up to the next $40.0 million; over $90.0 million shared equally.

2008: Up to $70.0 million shared equally, we are solely responsible for up to the next $30.0 million; over $100.0 million shared equally.

2009 and thereafter: All expenses shared equally.

Neither party will be reimbursed for any development expenses that it incurred prior to 2007.

We are obligated to use commercially reasonable efforts to supply clinical and commercial product requirements.

Bayer has the right to terminate the agreement without cause with at least six months or twelve months advance notice depending on defined circumstances at the time of termination. In the event of termination of the agreement for any reason, we retain all rights to the VEGF Trap-Eye.

Novartis Pharma AG

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 payment to us of $27.0 million.

IL-1 Trap development expenses incurred in 2003 were shared equally by Regeneron 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.

Table of Contents

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. 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.

Under the collaboration agreement, we retain the right to elect to collaborate in the future development and commercialization of a Novartis IL-1 antibody, which is in clinical development. Following completion of Phase 2 development and submission to us of a written report on the Novartis IL-1 antibody, we have the right, in consideration for an opt-in payment, to elect to co-develop and co-commercialize the Novartis IL-1 antibody in North America. If we elect to exercise this right, we are responsible for paying 45% of post-election North American development costs for the antibody product. In return, we are entitled to co-promote the Novartis IL-1 antibody and to receive 45% of net profits on sales of the antibody product in North America. Under certain circumstances, we are also entitled to receive royalties on sales of the Novartis IL-1 antibody in Europe.

In addition, under the collaboration agreement, Novartis has the right to elect to collaborate in the development and commercialization of a second generation IL-1 Trap following completion of its Phase 2 development, should we decide to clinically develop such a second generation product candidate. Novartis does not have any rights or options with respect to our IL-1 Trap currently in clinical development.

The Procter & Gamble Company

In May 1997, we entered into a long-term collaboration with Procter & Gamble to discover, develop, and commercialize pharmaceutical products, and Procter & Gamble agreed to provide funding in support of our research efforts related to the collaboration. Effective December 31, 2000, in accordance with the companies collaboration agreement, Procter & Gamble was obligated to fund our research on therapeutic areas that were of particular interest to Procter & Gamble through December 2005, with no further research obligations by either party thereafter. Under the collaboration agreement, research support from Procter & Gamble was $2.5 million per quarter, plus annual adjustments for inflation, through December 2005.

In June 2005, we and Procter & Gamble amended our collaboration agreement. Under the terms of the modified agreement, the two companies agreed that the research activities being pursued under the collaboration agreement were completed on June 30, 2005, six months prior to the December 31, 2005 expiration date in the collaboration agreement. Procter & Gamble agreed to make a one-time $5.6 million payment to Regeneron, which was received in July 2005, and to fund our research under the agreement through the second quarter of 2005. We agreed to pay Procter & Gamble approximately $1.0 million to acquire certain capital equipment owned by Procter & Gamble and located at our facilities. We and Procter & Gamble divided rights to research programs and preclinical product candidates that were developed during the research term of the collaboration. Neither party has the right to participate in the development or commercialization of the other party s product candidates. We are entitled to receive royalties based on any future product sales of a Procter & Gamble preclinical candidate arising from the collaboration, and Procter & Gamble is entitled to receive a small royalty on any sales of a single Regeneron candidate that is not currently being developed. Neither party is entitled to receive either royalties or other payments based on any other products arising from the collaboration.

Other Agreements

AstraZeneca

In February 2007, we entered into a non-exclusive license agreement with AstraZeneca that will allow AstraZeneca to utilize our VelocImmune® technology in its internal research programs to discover human monoclonal antibodies. Under the terms of the agreement, AstraZeneca made a $20.0 million non-refundable up-front payment to us. AstraZeneca also will make up to five additional annual payments of $20.0 million, subject to its ability to terminate the agreement after making the first three additional payments or earlier if the technology does not meet minimum performance criteria. We are entitled to receive a mid-single-digit royalty on any future sales of antibody products discovered by AstraZeneca using our VelocImmune technology.

Table of Contents

National Institutes of Health

In September 2006, we were awarded a five-year grant from the National Institutes of Health (NIH) as part of the NIH s Knockout Mouse Project. The goal of the Knockout Mouse Project is to build a comprehensive and broadly available resource of knockout mice to accelerate the understanding of gene function and human diseases. We will use our VelociGene® technology to take aim at 3,500 of the most difficult genes to target and which are not currently the focus of other large-scale knockout mouse programs. We have also agreed to grant a limited license to a consortium of research institutions, the other major participants in the Knockout Mouse Project, to use components of our VelociGene technology in the Knockout Mouse Project. We will generate a collection of targeting vectors and targeted mouse embryonic stem cells (ES cells) which can be used to produce knockout mice. These materials will be made widely available to academic researchers without charge. We will receive a fee for each targeted ES cell line or targeting construct made by us or the research consortium and transferred to commercial entities.

Under the NIH grant, we will be entitled to receive a minimum of $17.9 million over a five-year period. We will receive another $1.0 million to optimize our existing C57BL/6 ES cell line and its proprietary growth medium, both of which will be supplied to the research consortium for its use in the Knockout Mouse Project. We will have the right to use, for any purpose, all materials generated by us and the research consortium.

Accounting for Stock-based Employee Compensation

Effective January 1, 2005, we adopted the fair value based method of accounting for stock-based employee compensation under the provisions of Statement of Financial Accounting Standards No. (SFAS) 123, *Accounting for Stock-Based Compensation*, using the modified prospective method as described in SFAS 148, *Accounting for Stock-Based Compensation Transition and Disclosure.* As a result, in 2005, we recognized compensation expense, in an amount equal to the fair value of share-based payments (including stock option awards) on their date of grant, over the vesting period of the awards using graded vesting, which is an accelerated expense recognition method. Under the modified prospective method, compensation expense for Regeneron is recognized for (a) all share based payments granted on or after January 1, 2005 and (b) all awards granted to employees prior to January 1, 2005 that were unvested on that date. Prior to the adoption of the fair value method, we accounted for stock-based compensation to employees under the intrinsic value method of accounting set forth in Accounting Principles Board Opinion No. (APB) 25, *Accounting for Stock Issued to Employees*, and related interpretations. Therefore, compensation expense related to employee stock options was not reflected in operating expenses in any period prior to the first quarter of 2005 and prior period operating results have not been restated.

Effective January 1, 2006, we adopted the provisions of SFAS 123R, *Share-Based Payment*, which is a revision of SFAS 123. SFAS 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 123R requires companies to estimate the number of awards that are expected to be forfeited at the time of grant and to revise this estimate, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Effective January 1, 2005, and prior to our adoption of SFAS 123R, we recognized the effect of forfeitures in stock-based compensation cost in the period when they occurred, in accordance with SFAS 123. Upon adoption of SFAS 123R effective January 1, 2006, we were required to record a cumulative effect adjustment to reflect the effect of estimated forfeitures related to outstanding awards that are not expected to vest as of the SFAS 123R adoption date. This adjustment reduced our loss by $0.8 million and is included in our operating results for the year ended December 31, 2006 as a cumulative-effect adjustment of a change in accounting principle. Exclusive of the cumulative-effect adjustment, the effect of the change from applying the provisions of SFAS 123 to applying the provisions of SFAS 123R on our loss from operations, net loss, and net loss per share for the year ended December 31, 2006 was

not significant, and there was no impact to our cash flows for the year ended December 31, 2006.

Non-cash stock-based employee compensation expense related to stock option awards (Stock Option Expense) recognized in operating expenses totaled $18.4 million and $19.9 million for the years ended December 31, 2006 and 2005, respectively. In addition, for the year ended December 31, 2005, $0.1 million of Stock Option Expense

Table of Contents

was capitalized into inventory. As of December 31, 2006, there was $44.0 million of stock-based compensation cost related to outstanding nonvested stock options, net of estimated forfeitures, which had not yet been recognized in operating expenses. We expect to recognize this compensation cost over a weighted-average period of 1.9 years. In addition, there are 723,092 options which are unvested as of December 31, 2006 and would become vested upon our products achieving certain sales targets and the optionee satisfying certain service conditions. Potential compensation cost, measured on the grant date, related to these performance options totals $2.7 million and will begin to be recognized only if, and when, these options performance condition is considered to be probable of attainment.

Assumptions

We use the Black-Scholes model to estimate the fair value of each option granted under the Regeneron Pharmaceuticals, Inc. 2000 Long-Term Incentive Plan. Using this model, fair value is calculated based on assumptions with respect to (i) expected volatility of our Common Stock price, (ii) the periods of time over which employees and members of our board of directors are expected to hold their options prior to exercise (expected lives), (iii) expected dividend yield on our Common Stock, and (iv) risk-free interest rates, which are based on quoted U.S. Treasury rates for securities with maturities approximating the options expected lives. Expected volatility has been estimated based on actual movements in our stock price over the most recent historical periods equivalent to the options expected lives. Expected lives are principally based on our limited historical exercise experience with option grants with similar exercise prices. The expected dividend yield is zero as we have never paid dividends and do not currently anticipate paying any in the foreseeable future. The following table summarizes the weighted average values of the assumptions we used in computing the fair value of option grants during 2006, 2005 and 2004:

	2006	2005	2004
Expected volatility	67%	71%	80%
Expected lives from grant date	6.5 years	5.9 years	7.5 years
Expected dividend yield	0%	0%	0%
Risk-free interest rate	4.51%	4.16%	4.03%

Changes in any of these estimates may materially affect the fair value of stock options granted and the amount of stock-based compensation recognized in any period.

Results of Operations

Years Ended December 31, 2006 and 2005

Net Loss:

Regeneron reported a net loss of $102.3 million, or $1.77 per share (basic and diluted) for the year ended December 31, 2006, compared to a net loss of $95.4 million, or $1.71 per (basic and diluted) for 2005.

Revenues:

Revenues for the years ended December 31, 2006 and 2005 consist of the following:

	2006	2005
	(In millions)	

Contract research & development revenue		
Sanofi-aventis	$ 47.8	$ 43.4
Procter & Gamble		6.0
Other	3.3	3.1
Total contract research & development revenue	51.1	52.5
Contract manufacturing revenue	12.3	13.7
Total revenue	$ 63.4	$ 66.2

Table of Contents

We recognize revenue from sanofi-aventis, in connection with the companies VEGF Trap collaboration, 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) (see Critical Accounting Policies and Significant Judgments and Estimates). We earn contract research and development revenue from sanofi-aventis which, as detailed below, consists partly of reimbursement for research and development expenses and partly of the recognition of revenue related to a total of $105.0 million of non-refundable, up-front payments received in 2003 and 2006. Non-refundable up-front payments are recorded as deferred revenue and recognized ratably over the period during which we are obligated to perform services.

Sanofi-aventis Contract Research & Development Revenue	**December 31, 2006**	**2005**
	(In millions)	
Regeneron expense reimbursement	$ 36.4	$ 33.9
Recognition of deferred revenue related to up-front payments	11.4	9.5
Total	$ 47.8	$ 43.4

Sanofi-aventis reimbursement of Regeneron VEGF Trap expenses increased in 2006 compared to 2005, primarily due to higher costs related to our manufacture of VEGF Trap clinical supplies during the first half of 2006. Recognition of deferred revenue related to sanofi-aventis up-front payments also increased in 2006 from the same period in 2005, due to our receipt in January 2006 of a $25.0 million non-refundable, up-front payment from sanofi-aventis related to the expansion of the companies VEGF Trap collaboration to include Japan. As of December 31, 2006, $70.0 million of the original $105.0 million of up-front payments was deferred and will be recognized as revenue in future periods.

Contract research and development revenue earned from Procter & Gamble decreased in 2006 compared to 2005, as the research activities being pursued under our December 2000 collaboration agreement with Procter & Gamble, as amended, were completed on June 30, 2005, as described above under Collaborations The Procter & Gamble Company. Since the second quarter of 2005, we have not received, and do not expect to receive, any further contract research and development revenue from Procter & Gamble.

As described above, in October 2006 we entered into a VEGF Trap-Eye collaboration with Bayer. We will recognize revenue from Bayer, in connection with the companies collaboration, in accordance with SAB 104 and EITF 00-21. When we and Bayer have formalized our projected global development plans for the VEGF Trap-Eye, as well as the projected responsibilities of each of the companies under those development plans, we will begin recognizing contract research and development revenue related to payments from Bayer. As a result, there was no contract research and development revenue earned from Bayer in 2006. As of December 31, 2006, the $75.0 million up-front payment received from Bayer in October 2006 was deferred and will be recognized as revenue in future periods.

Other contract research and development revenue includes $0.5 million recognized in connection with our NIH Grant, as described above.

Contract manufacturing revenue relates to our long-term agreement with Merck & Co., Inc., which expired in October 2006, to manufacture a vaccine intermediate at our Rensselaer, New York facility. Contract manufacturing revenue decreased in 2006 compared to 2005 due to a decrease in product shipments to Merck in 2006. Revenue and the related manufacturing expense were recognized as product was shipped, after acceptance by Merck. Included in

contract manufacturing revenue in 2006 and 2005 were $1.2 million and $1.4 million, respectively, of deferred revenue associated with capital improvement reimbursements paid by Merck prior to commencement of production. We do not expect to receive any further contract manufacturing revenue from Merck and there was no Merck deferred revenue as of the end of 2006.

Expenses:

Total operating expenses decreased to $171.1 million in 2006 from $190.6 million in 2005 due, in part, to our lower headcount, as described above. (Also see Severance Costs below.)

Table of Contents

Operating expenses in 2006 and 2005 include a total of $18.4 million and $19.9 million of Stock Option Expense, respectively, as detailed below:

	For the Year Ended December 31, 2006		
Expenses	**Expenses Before Inclusion of Stock Option Expense**	**Stock Option Expense**	**Expenses as Reported**
		(In millions)	
Research and development	$ 126.9	$ 10.2	$ 137.1
Contract manufacturing	7.8	0.3	8.1
General and administrative	18.0	7.9	25.9
Total operating expenses	$ 152.7	$ 18.4	$ 171.1

	For the Year Ended December 31, 2005		
Expenses	**Expenses Before Inclusion of Stock Option Expense**	**Stock Option Expense**	**Expenses as Reported**
		(In millions)	
Research and development	$ 143.7	$ 11.9	$ 155.6
Contract manufacturing	9.2	0.4	9.6
General and administrative	17.8	7.6	25.4
Total operating expenses	$ 170.7	$ 19.9	$ 190.6

Research and Development Expenses:

Research and development expenses decreased to $137.1 million for the year ended December 31, 2006 from $155.6 million for 2005. The following table summarizes the major categories of our research and development expenses for the years ended December 31, 2006 and 2005:

	Year Ended December 31,		
Research and Development Expenses	**2006**	**2005 (1)**	**Increase (Decrease)**
		(In millions)	

Payroll and benefits (2)	$ 44.8	$ 53.6	$ (8.8)
Clinical trial expenses	14.9	18.2	(3.3)
Clinical manufacturing costs (3)	39.2	41.6	(2.4)
Research and preclinical development costs	17.5	19.2	(1.7)
Occupancy and other operating costs	20.7	23.0	(2.3)
Total research and development	$ 137.1	$ 155.6	$ (18.5)

(1) For the major categories of research and development expenses, amounts for the year ended December 31, 2005 have been reclassified to conform with, and be comparable to, the current year s presentation. Total research and development expenses for the year ended December 31, 2005 are unchanged from amounts previously reported.

(2) Includes $8.4 million and $10.5 million of Stock Option Expense for the years ended December 31, 2006 and 2005, respectively.

(3) Represents the full cost of manufacturing drug for use in research, preclinical development, and clinical trials, including related payroll and benefits, Stock Option Expense, manufacturing materials and supplies, depreciation, and occupancy costs of our Rensselaer manufacturing facility. Includes $1.8 million and $1.4 million of Stock Option Expense for the years ended December 31, 2006 and 2005, respectively.

Payroll and benefits decreased principally due to our lower headcount in 2006. In addition, payroll and benefits in 2006 and 2005 included $0.4 million and $2.2 million, respectively, of severance costs associated with our

Table of Contents

workforce reduction plan that we initiated in October 2005. Clinical trial expenses decreased primarily due to lower IL-1 Trap costs in 2006 as we discontinued clinical development of the IL-1 Trap in adult rheumatoid arthritis and osteoarthritis in the second half of 2005. This decrease was partly offset by higher 2006 VEGF Trap-Eye costs related to Phase 1 and Phase 2 clinical trials that we are conducting in wet AMD. Clinical manufacturing costs decreased because of lower costs in 2006 related to manufacturing IL-1 Trap clinical supplies, which were partially offset by higher costs related to manufacturing VEGF Trap clinical supplies. Research and preclinical development costs decreased principally because of lower costs for general research supplies in 2006 as we narrowed the focus of our research and development efforts due, in part, to the expiration of our collaboration with Procter & Gamble in June 2005, as described above. Occupancy and other operating costs decreased primarily due to our lower 2006 headcount and lower costs for utilities associated with our leased research facilities in Tarrytown, New York.

Contract Manufacturing Expenses:

Contract manufacturing expenses decreased to $8.1 million in 2006, compared to $9.6 million in 2005, primarily because we shipped less product to Merck in 2006.

General and Administrative Expenses:

General and administrative expenses increased to $25.9 million in 2006 from $25.4 million in the same period of 2005 as higher legal expenses related to general corporate matters and higher patent-and trademark-related costs were partly offset by lower professional fees for internal audit and other administrative advisory services and lower administrative facility costs.

Other Income and Expense:

In June 2005, we and Procter & Gamble amended our collaboration agreement and agreed that the research activities of both companies under the collaboration agreement were completed. In connection with the amendment, Procter & Gamble made a one-time $5.6 million payment to us, which we recognized as other contract income in 2005. In January 2005, we and sanofi-aventis amended our collaboration agreement to exclude rights to develop and commercialize the VEGF Trap for intraocular delivery to the eye. In connection with the amendment, sanofi-aventis made a one-time $25.0 million payment to us, which we recognized as other contract income in 2005.

Investment income increased to $16.5 million in 2006 from $10.4 million in 2005, due primarily to higher balances of cash and marketable securities (due, in part, to the up-front payment received from Bayer in October 2006, as described above, and the receipt of net proceeds from the November 2006 public offering of our Common Stock), as well as higher effective interest rates on investment securities in 2006. Interest expense was $12.0 million in 2006 and 2005. 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, 2005 and 2004

Net Income (Loss):

Regeneron reported a net loss of $95.4 million, or $1.71 per share (basic and diluted) for the year ended December 31, 2005, compared with net income of $41.7 million, or $0.75 per basic share and $0.74 per diluted share, for 2004. Our net loss in 2005 included $19.9 million of Stock Option Expense due to our adoption of SFAS 123 effective January 1, 2005, as described above.

Table of Contents

Revenues:

Revenues for the years ended December 31, 2005 and 2004 consist of the following:

	2005	2004
	(In millions)	
Contract research & development revenue		
Sanofi-aventis	$ 43.4	$ 78.3
Novartis		22.1
Procter & Gamble	6.0	10.5
Other	3.1	2.2
Total contract research & development revenue	52.5	113.1
Research progress payments		
Sanofi-aventis		25.0
Novartis		17.8
Total research progress payments		42.8
Contract manufacturing revenue	13.7	18.1
Total revenue	$ 66.2	$ 174.0

Our total revenue decreased to $66.2 million in 2005 from $174.0 million in 2004, due primarily to lower revenues related to our collaboration with sanofi-aventis on the VEGF Trap and the absence in the 2005 period of revenues related to our collaboration with Novartis on the IL-1 Trap which ended in 2004. We recognize revenue from the sanofi-aventis and Novartis collaborations in accordance with SAB 104 and EITF 00-21 (see Critical Accounting Policies and Significant Judgments and Estimates). 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 during which we are obligated to perform services.

Contract research & development revenues earned from sanofi-aventis and Novartis for 2005 and 2004 were as follows:

		Up-front Payments to Regeneron		
2005 Regeneron Expense Reimbursement	Total Payments	Amount Recognized in 2005	Deferred Revenue at December 31, 2005	Total Revenue Recognized in 2005

	(In millions)				
Sanofi-aventis	$ 33.9	$ 105.0	$ 9.5	$ 81.3	$ 43.4

	Up-front Payments to Regeneron				
	2004 Regeneron Expense Reimbursement	Total Payment	Amount Recognized in 2004	Deferred Revenue at December 31, 2004	Total Revenue Recognized in 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

Sanofi-aventis reimbursement of Regeneron VEGF Trap expenses decreased in 2005 compared to 2004, primarily due to lower clinical supply manufacturing costs in 2005. We manufactured clinical supplies of the VEGF Trap throughout 2004, but only manufactured VEGF Trap clinical supplies during the fourth quarter of 2005. 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 received from Novartis in March 2003 was

Table of Contents

recognized as contract research and development revenue. Since the first quarter of 2004, we have not received, and do not expect to receive, any further contract research and development revenue from Novartis.

Contract research and development revenue earned from Procter & Gamble also decreased in 2005 compared to 2004, resulting from the June 2005 amendment to our December 2000 collaboration agreement with Procter & Gamble. Under the terms of the modified agreement, Procter & Gamble funded Regeneron s research for the first two quarters of 2005, compared with a full year of collaborative research funding in 2004. Since the second quarter of 2005, we have not received, and do not expect to receive, any further contract research and development revenue from Procter & Gamble.

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 of 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, which expired in October 2006. Contract manufacturing revenue decreased to $13.7 million in 2005 from $18.1 million in 2004, principally due to a decrease in product shipments to Merck in 2005 compared to 2004. Revenue and the related manufacturing expense were recognized as product was shipped, after acceptance by Merck. Included in contract manufacturing revenue in 2005 and 2004 were $1.4 million and $3.6 million, respectively, of deferred revenue associated with capital improvement reimbursements paid by Merck prior to commencement of production.

Expenses:

Total operating expenses increased to $190.6 million in 2005 from $168.4 million in 2004. Operating expenses in 2005 include a total of $19.9 million of Stock Option Expense, as follows:

	For the Year Ended December 31,			
	2005			2004
Expenses	Expenses Before Inclusion of Stock Option Expense	Stock Option Expense	Expenses as Reported	Expenses as Reported
	(In millions)			
Research and development	$ 143.7	$ 11.9	$ 155.6	$ 136.1
Contract manufacturing	9.2	0.4	9.6	15.2
General and administrative	17.8	7.6	25.4	17.1
Total operating expenses	$ 170.7	$ 19.9	$ 190.6	$ 168.4

In addition, $0.1 million of Stock Option Expense was capitalized into inventory, for a total of $20.0 million of Stock Option Expense recognized during the year ended December 31, 2005. As described under Accounting for Stock-based Employee Compensation above, Stock Option Expense was not included in operating expenses in 2004,

as reported in our Statement of Operations. In 2004, had we adopted the fair value based method of accounting for stock-based employee compensation under the provisions of SFAS 123, Stock Option Expense would have totaled $33.6 million. The decrease in total Stock Option Expense of $13.6 million in 2005 was partly due to lower exercise prices of annual employee option grants made by us in December 2004 in comparison to the exercise prices of annual grants in recent prior years. Exercise prices of these option grants were generally equal to the fair market value of our Common Stock on the date of grant. The decrease in Stock Option Expense in 2005 was also due, in part, to the exchange of options by eligible employees in connection with our stock option exchange program in January 2005, as the unamortized fair value of the surrendered options on the date of the exchange is being recognized as Stock Option Expense over a longer time period (the vesting period of the replacement options) in accordance with SFAS 123.

Table of Contents

Research and Development Expenses:

Research and development expenses increased to $155.6 million for the year ended December 31, 2005 from $136.1 million for 2004 due, in part, to the inclusion of $11.9 million of Stock Option Expense in 2005 research and development expenses, resulting from the adoption of SFAS 123, effective January 1, 2005. The following table summarizes the major categories of our research and development expenses for the years ended December 31, 2005 and 2004:

	For the Year Ended December 31,							
	2005 (1)						2004 (1)(2)	
Research and Development Expenses	Expenses Before Inclusion of Stock Option Expense		Stock Option Expense		Expenses as Reported		Expenses as Reported	
	(In millions)							
Payroll and benefits	$	43.1	$	10.5	$	53.6	$	38.6
Clinical trial expenses		18.2				18.2		10.3
Clinical manufacturing costs (3)		40.2		1.4		41.6		42.8
Research and preclinical development costs		19.2				19.2		22.2
Occupancy and other operating costs		23.0				23.0		22.2
Total research and development	$	143.7	$	11.9	$	155.6	$	136.1

(1) For the major categories of research and development expenses, amounts for the years ended December 31, 2005 and 2004 have been reclassified to conform with, and be comparable to, the current year s presentation. Total research and development expenses for the years ended December 31, 2005 and 2004 are unchanged from amounts previously reported.

(2) In 2004, research and development expenses as reported in our Statement of Operations did not include Stock Option Expense.

(3) 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, occupancy costs of our Rensselaer manufacturing facility, and, in 2005 only, Stock Option Expense.

Payroll and benefits, exclusive of Stock Option Expense, increased $4.5 million in 2005 from 2004 due primarily to 2005 wage and salary increases, higher employee benefit costs, and severance costs (totaling $2.2 million in 2005) associated with our workforce reduction plan that we initiated in October 2005. Clinical trial expenses increased $7.9 million in 2005 from 2004 due primarily to higher IL-1 Trap costs associated with commencing clinical studies in new indications and discontinuing the Phase 2b study in adult rheumatoid arthritis. Clinical manufacturing costs, exclusive of Stock Option Expense, decreased $2.6 million in 2005 from 2004, as lower costs in 2005 related to manufacturing clinical supplies of the VEGF Trap and the IL-4/13 Trap were partly offset by higher costs related to

manufacturing clinical supplies of the IL-1 Trap. Research and preclinical development costs decreased $3.0 million in 2005 from 2004 due primarily to lower VEGF Trap preclinical development costs and lower costs for general research supplies in 2005. Occupancy and other operating costs increased $0.8 million in 2005 from 2004, due primarily to higher costs for utilities, taxes, and operating expenses associated with our leased research facilities in Tarrytown, New York.

Contract Manufacturing Expenses:

Contract manufacturing expenses decreased to $9.6 million in 2005, compared to $15.2 million in 2004, primarily because we shipped less product to Merck in 2005 and we incurred unfavorable manufacturing costs in 2004, which were expensed in the period incurred.

General and Administrative Expenses:

General and administrative expenses increased to $25.4 million in 2005 from $17.1 million in 2004, due primarily to the inclusion of $7.6 million of Stock Option Expense in 2005 general and administrative expenses,

Table of Contents

resulting from the adoption of SFAS 123, effective January 1, 2005. In addition, in 2005 administrative wage and salary increases, higher employee benefits costs and higher administrative facility costs were partly offset by (i) lower legal expenses related to Company litigation and general corporate matters and (ii) lower professional fees, principally associated with accounting and other services related to our first year of compliance in 2004 with the requirements of Section 404 of the Sarbanes-Oxley Act of 2002.

Other Income and Expense:

In June 2005, we and Procter & Gamble amended our collaboration agreement and agreed that the research activities of both companies under the collaboration agreement were completed. In connection with the amendment, Procter & Gamble made a one-time $5.6 million payment to us, which we recognized as other contract income in 2005. In January 2005, we and sanofi-aventis amended our collaboration agreement to exclude rights to develop and commercialize the VEGF Trap for intraocular delivery to the eye. In connection with the amendment, sanofi-aventis made a one-time $25.0 million payment to us, which we recognized as other contract income in 2005. In the first quarter of 2004, Novartis notified us of its decision to forgo its right under the collaboration to jointly develop the IL-1 Trap and subsequently paid 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 2004.

Investment income increased to $10.4 million in 2005 from $5.5 million in 2004, due primarily to higher effective interest rates on investment securities in 2005. Interest expense decreased slightly to $12.0 million in 2005 from $12.2 million in 2004. 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 sanofi-aventis, Bayer, and Merck, and investment income.

Years Ended December 31, 2006 and 2005

At December 31, 2006, we had $522.9 million in cash, cash equivalents, and marketable securities compared with $316.7 million at December 31, 2005. In January 2006, we received a $25.0 million up-front payment from sanofi-aventis, which was receivable at December 31, 2005, in connection with an amendment to our collaboration agreement to include Japan. In October 2006, we received a $75.0 million up-front payment in connection with our new VEGF Trap-Eye license and collaboration agreement with Bayer. In November 2006, we completed a public offering of 7.6 million shares of our Common Stock and received proceeds, after expenses, of $174.6 million.

Cash Provided by (Used in) Operations:

Net cash provided by operations was $23.1 million in 2006, compared to net cash used in operations of $30.3 million in 2005. Our net losses of $102.3 million in 2006 and $95.4 million in 2005 included $18.7 million and $21.9 million, respectively, of non-cash stock-based employee compensation costs, of which $18.4 million and $19.9 million, respectively, represented Stock Option Expense resulting from the adoption of SFAS 123R in January 2006 and SFAS 123 in January 2005. In 2006, end-of-year accounts receivable balances decreased by $29.0 million compared to 2005, due to the January 2006 receipt of the $25.0 million up-front payment from sanofi-aventis, as described above, and lower amounts due from sanofi aventis for reimbursement of VEGF Trap development expenses. Also, our

deferred revenue balances increased by $60.8 million in 2006 compared to 2005, due primarily to the October 2006 $75.0 million up-front payment from Bayer, as described above, partly offset by 2006 revenue recognition of $11.4 million from deferred sanofi-aventis up-front payments. In 2005, end-of-year accounts receivable balances decreased by $6.6 million compared to 2004, due to lower amounts due from sanofi-aventis for reimbursement of VEGF Trap development expenses and the June 2005 completion of funding for Regeneron research activities under our collaboration with Procter & Gamble. Also, our deferred revenue balances increased

Table of Contents

by $14.5 million in 2005 compared to 2004, due primarily to the January 2006 $25.0 million up-front payment from sanofi-aventis, which was receivable at December 31, 2005, partly offset by 2005 revenue recognition of $9.5 million from deferred sanofi-aventis up-front payments. The majority of cash used in our operations in both 2006 and 2005 was to fund research and development, primarily related to our clinical programs.

In both 2006 and 2005, we made two semi-annual interest payments totaling $11.0 million per year on our convertible senior subordinated notes.

Cash Provided by Investing Activities:

Net cash used in investing activities was $155.1 million in 2006 compared to net cash provided by investing activities of $115.5 million in 2005, due primarily to an increase in purchases of marketable securities net of sales or maturities. In 2006, purchases of marketable securities exceeded sales or maturities by $150.7 million, whereas in 2005, sales or maturities of marketable securities exceeded purchases by $120.5 million.

Cash Provided by Financing Activities:

Cash provided by financing activities increased to $185.4 million in 2006 from $4.1 million in 2005 due primarily to our completed public offering of 7.6 million shares of Common Stock in November 2006, as described above. In addition, proceeds from issuances of Common Stock in connection with exercises of employee stock options increased from $4.1 million in 2005 to $10.4 million in 2006.

Collaboration with the sanofi-aventis Group:

Under our collaboration agreement with sanofi-aventis, as described under Collaborations above, agreed upon worldwide VEGF Trap 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 be obligated to 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 and Japan royalties, or at a faster rate at our option. In addition, if the first commercial sale of a VEGF Trap product for intraocular delivery to the eye 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. Since inception of the collaboration agreement through December 31, 2006, we and sanofi-aventis have incurred $205.0 million in agreed upon development expenses related to the VEGF Trap program. We and sanofi-aventis plan to initiate in 2007 multiple additional clinical studies to evaluate the VEGF Trap as both a single agent and in combination with other therapies in various cancer indications.

Sanofi-aventis funded $47.8 million, $43.4 million, and $67.8 million, respectively, of our VEGF Trap development costs in 2006, 2005, and 2004, of which $6.8 million, $10.5 million, and $13.9 million, respectively, were included in accounts receivable as of December 31, 2006, 2005, and 2004. In addition, we have received up-front payments of $80.0 million in September 2003 and $25.0 million in January 2006 from sanofi-aventis in connection with our collaboration. Both up-front payments were recorded to deferred revenue and are being recognized as contract research and development revenue ratably over the period during which we expect to perform services. In 2006 and 2005, we recognized $11.4 million and $9.5 million of revenue, respectively, related to these up-front payments.

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.

Table of Contents

Collaboration with Bayer Healthcare:

Under our collaboration agreement with Bayer, as described under Collaborations above, agreed upon VEGF Trap-Eye development expenses incurred by both companies, beginning in 2007, under a global development plan, will be shared as follows:

2007: Up to $50.0 million shared equally; we are solely responsible for up to the next $40.0 million; over $90.0 million shared equally.

2008: Up to $70.0 million shared equally, we are solely responsible for up to the next $30.0 million; over $100.0 million shared equally.

2009 and thereafter: All expenses shared equally.

Neither party will be reimbursed for any development expenses that it incurred prior to 2007.

We are obligated to use commercially reasonable efforts to supply clinical and commercial product requirements.

If the VEGF Trap-Eye is granted marketing authorization in a major market country outside the United States and the collaboration becomes profitable, we will be obligated to reimburse Bayer out of our share of the collaboration profits for 50% of the agreed upon development expenses that Bayer has incurred in accordance with a formula based on the amount of development expenses that Bayer has incurred and our share of the collaboration profits, or at a faster rate at our option. In wet AMD, we and Bayer plan in 2007 to complete our Phase 2 clinical study of the VEGF Trap-Eye currently in progress and to initiate the Phase 3 clinical program.

In October 2006, we received a $75.0 million up-front payment from Bayer in connection with our collaboration, which was recorded to deferred revenue. When we and Bayer have formalized our projected global development plans for the VEGF Trap-Eye, as well as the projected responsibilities of each of the companies under those development plans, we will begin recognizing revenue related to payments from Bayer.

Bayer has the right to terminate the agreement without cause with at least six months or twelve months advance notice depending on defined circumstances at the time of termination. In the event of termination of the agreement for any reason, we retain all rights to the VEGF Trap-Eye.

National Institutes of Health Grant:

Under our five-year grant from the NIH, as described under Other Agreements above, we will be entitled to receive a minimum of $17.9 million over a five-year period, subject to compliance with the grant s terms and annual funding approvals, and another $1.0 million to optimize our existing C57BL/6 ES cell line and its proprietary growth medium. In 2006, we recognized $0.5 million of revenue related to the NIH Grant, which was receivable at the end of 2006. In 2007, we expect to receive funding of approximately $5 million for reimbursement of Regeneron expenses related to the NIH Grant.

License Agreement with AstraZeneca:

Under our non-exclusive license agreement with AstraZeneca, as described under Other Agreements above, AstraZeneca made a $20.0 million non-refundable up-front payment to us in February 2007. AstraZeneca also will make up to five additional annual payments of $20.0 million, subject to its ability to terminate the agreement after

making the first three additional payments or if the technology does not meet minimum performance criteria.

Severance Costs:

In September 2005, we announced plans to reduce our workforce by approximately 165 employees in connection with narrowing the focus of our research and development efforts, substantial improvements in manufacturing productivity, the September 2005 expiration of our collaboration with Procter & Gamble, and the completion of contract manufacturing for Merck in late 2006. The majority of the headcount reduction occurred in the fourth quarter of 2005. The remaining headcount reductions occurred in 2006 as we completed activities related to contract manufacturing for Merck.

Table of Contents

Costs associated with the workforce reduction were comprised principally of severance payments and related payroll taxes, employee benefits, and outplacement services. Termination costs related to 2005 workforce reductions were expensed in the fourth quarter of 2005, and included $0.2 million of non-cash expenses. Estimated termination costs associated with the workforce reduction in 2006 were measured in October 2005 and expensed ratably over the expected service period of the affected employees in accordance with SFAS 146, *Accounting for Costs Associated with Exit or Disposal Activities.* Total costs associated with the 2005 and 2006 workforce reductions were $2.6 million, of which $2.2 million was charged to expense in the fourth quarter of 2005 and $0.4 million was charged to expense in 2006.

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.

New Operating Lease Tarrytown, New York Facilities

In December 2006, we entered into a new operating lease agreement for approximately 221,000 square feet of laboratory and office space at our current Tarrytown location. The new lease includes approximately 27,000 square feet that we currently occupy (our retained facilities) and approximately 194,000 square feet to be located in new facilities that will be constructed and which are expected to be completed in early-2009. The term of the lease is expected to commence in early 2008 and will expire approximately 16 years later. Under the new lease we also have various options and rights on additional space at the Tarrytown site, and will continue to lease our present facilities until the new facilities are ready for occupancy. In addition, the lease contains three renewal options to extend the term of the lease by five years each and early termination options for our retained facilities only. The lease provides for monthly payments over the term of the lease related to our retained facilities, the costs of construction and tenant improvements for our new facilities, and additional charges for utilities, taxes, and operating expenses.

In connection with the new lease agreement, in December 2006, we issued a letter of credit in the amount of $1.6 million to our landlord, which is collateralized by a $1.6 million bank certificate of deposit.

Capital Expenditures:

Our additions to property, plant, and equipment totaled $3.3 million in 2006, $4.7 million in 2005, and $6.0 million in 2004. In 2007, we expect to incur approximately $15 million in capital expenditures primarily to support our manufacturing, development, and research activities.

Funding Requirements:

Our total expenses for research and development from inception through December 31, 2006 have been approximately $1,150 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 those with sanofi-aventis and Bayer, and agreements to use our Velocigene® technology platform. We incurred expenses associated with these agreements, which include an allocable portion of general and administrative costs, of $43.4 million, $42.2 million, and $75.3 million in 2006, 2005, and 2004, respectively.

We expect to continue to incur substantial funding requirements primarily for research and development activities (including preclinical and clinical testing). Before taking into account reimbursements from collaborators, we currently anticipate that approximately 55%-65% of our expenditures for 2007 will be directed toward the preclinical and clinical development of product candidates, including the IL-1 Trap, VEGF Trap, VEGF Trap-Eye, and monoclonal antibodies; approximately 15%-25% of our expenditures for 2007 will be applied to our basic research activities and the continued development of our novel technology platforms; and the remainder of our expenditures for 2007 will be used for capital expenditures and general corporate purposes.

Table of Contents

In connection with our funding requirements, the following table summarizes our contractual obligations as of December 31, 2006 for leases and long-term debt.