

REGENERON PHARMACEUTICALS INC  
Form 10-K  
February 21, 2012

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

**FORM 10-K**

(Mark One)

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

(X)  
OR

For the fiscal year ended December 31, 2011

( )

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  
(State or other jurisdiction of  
incorporation or organization)

13-3444607  
(I.R.S. Employer Identification No)

777 Old Saw Mill River Road, Tarrytown, New York  
(Address of principal executive offices)

10591-6707  
(Zip code)

(914) 847-7000  
(Registrant's telephone number, including area code)

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

Title of each class	Name of each exchange on which registered
Common Stock - par value \$.001 per share	NASDAQ Global Select Market

Securities registered pursuant to section 12(g) of the Act: None

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

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

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes  No \_\_\_\_\_

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

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

Large accelerated filer  Accelerated filer  Non-accelerated filer  Smaller reporting company

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

The aggregate market value of the common stock held by non-affiliates of the registrant was approximately \$4,913,223,000, computed by reference to the closing sales price of the stock on NASDAQ on June 30, 2011, 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 10, 2012:

Class of Common Stock	Number of Shares
Class A Stock, \$.001 par value	2,109,512
Common Stock, \$.001 par value	91,779,465

### DOCUMENTS INCORPORATED BY REFERENCE:

Specified portions of the Registrant's definitive proxy statement to be filed in connection with solicitation of proxies for its 2012 Annual Meeting of Shareholders are incorporated by reference into Part III of this Form 10-K. Exhibit index is located on pages 79 to 82 of this filing.

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## PART I

## ITEM 1. BUSINESS

*This Annual Report on Form 10-K contains forward-looking statements that involve risks and uncertainties relating to future events and the future financial performance of Regeneron Pharmaceuticals, Inc., and actual events or results may differ materially from these forward-looking statements. These statements concern, and these risks and uncertainties include, among other things, the success of our commercialization of EYLEA<sup>®</sup>, the nature, timing, and possible success of and therapeutic applications for our product candidates and research programs now underway or planned, the likelihood and timing of possible regulatory approval and commercial launch of our late-stage product candidates, determinations by regulatory and administrative governmental authorities which may delay or restrict our ability to continue to develop or commercialize our product and drug candidates, competing drugs that may be superior to our product and drug candidates, uncertainty of market acceptance of our product and drug candidates, unanticipated expenses, the availability and cost of capital, the costs of developing, producing, and selling products, the potential for any collaboration agreement, including our agreements with Sanofi and Bayer HealthCare LLC, to be canceled or terminated without any product success, and risks associated with third-party intellectual property and pending or future litigation relating thereto. These statements are made by us based on management's current beliefs and judgment. In evaluating such statements, shareholders and potential investors should specifically consider the various factors identified under the caption Risk Factors which could cause actual events and 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 fully integrated biopharmaceutical company that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. We currently have two marketed products:

- EYLEA<sup>®</sup> (aflibercept) Injection, known in the scientific literature as VEGF Trap-Eye, which is available in the United States for the treatment of neovascular age-related macular degeneration (wet AMD). Wet AMD is the leading cause of acquired blindness for people over the age of 65 in the United States and Europe; and
- ARCALYST<sup>®</sup> (rilonacept) Injection for Subcutaneous Use, which is available by prescription in the United States for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS), including Familial Cold Auto-inflammatory Syndrome (FCAS) and Muckle-Wells Syndrome (MWS) in adults and children 12 and older.

We have 13 product candidates in clinical development, all of which were discovered in our research laboratories. Our Trap-based, late-stage programs are:

- EYLEA<sup>®</sup>, which is being developed for the treatment of additional serious eye diseases;
- ZALTRAP<sup>®</sup> (aflibercept), known in the scientific literature as VEGF Trap, which is being developed in oncology in collaboration with Sanofi; and
- ARCALYST<sup>®</sup>, which is being developed for the prevention of gout flares in patients initiating uric acid-lowering treatment.

Our antibody-based clinical programs include the following fully human monoclonal antibodies:

- Sarilumab (REGN88), an antibody to the interleukin-6 receptor (IL-6R), which is being developed in rheumatoid arthritis;
- REGN727, an antibody to Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9), which is being developed for low-density lipoprotein (LDL) cholesterol reduction;
- REGN668, an antibody to the interleukin-4 receptor (IL-4R), which is being developed in atopic dermatitis and eosinophilic asthma;
- REGN421, an antibody to Delta-like ligand-4 (Dl14), a novel angiogenesis target, which is being developed in oncology;
- REGN910, an antibody to Angiopoietin-2 (ANG2), another novel angiogenesis target, which is being developed in oncology;
- REGN475, an antibody to Nerve Growth Factor (NGF), which is being developed for the treatment of pain (currently on clinical hold);
- REGN728, an antibody in clinical development against an undisclosed target;

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- REGN1033, an antibody in clinical development against an undisclosed target;
- REGN846, an antibody in clinical development against an undisclosed target, which is being developed in atopic dermatitis; and
- REGN1154, an antibody in clinical development against an undisclosed target.

With the exception of REGN475, REGN846, and REGN1154, which we are developing independently, all of these antibodies are being developed in collaboration with Sanofi.

Our core business strategy is to maintain a strong foundation in basic scientific research and discovery-enabling technologies, to combine that foundation with our clinical development and manufacturing capabilities, and to continue to expand our commercialization capabilities in anticipation of possible regulatory approval and launch of one or more of our late-stage product candidates. Our long-term objective is to build a successful, integrated, multi-product biopharmaceutical company that provides patients and medical professionals with innovative options for preventing and treating human diseases.

We believe that our ability to develop product candidates is enhanced by the application of our *VelociSuite* technology platforms. Our discovery platforms are designed to identify specific proteins of therapeutic interest for a particular disease or cell type and validate these targets through high-throughput production of genetically modified mice using our *VelociGene*<sup>®</sup> technology to understand the role of these proteins in normal physiology, as well as in models of disease. Our human monoclonal antibody technology (*VelocImmune*<sup>®</sup>) and cell line expression technologies (*VelociMab*<sup>®</sup>) may then be utilized to discover and produce new product candidates directed against the disease target. Our antibody product candidates currently in clinical trials were developed using *VelocImmune*<sup>®</sup>. Under the terms of our antibody collaboration with Sanofi, which was expanded during 2009, we plan to advance a total of 20 to 30 candidates into clinical development over the life of the agreement. We continue to invest in the development of enabling technologies to assist in our efforts to identify, develop, manufacture, and commercialize new product candidates.

#### **Commercial Products:**

##### ***EYLEA*<sup>®</sup>(*aflibercept*) Injection    *wet AMD***

In November 2011, we received U.S. marketing approval from the U.S. Food and Drug Administration (FDA) for EYLEA<sup>®</sup> Injection for the treatment of patients with wet AMD. The approval of EYLEA<sup>®</sup> was granted by the FDA under a Priority Review, a designation that is given to drugs that offer major advances in treatment, or provide a treatment where no adequate therapy exists. Net product sales of EYLEA<sup>®</sup> in 2011 were \$24.8 million.

EYLEA<sup>®</sup>, known in the scientific literature as VEGF Trap-Eye, is a fusion protein locally administered in the eye that is designed to bind Vascular Endothelial Growth Factor-A (VEGF-A) and Placental Growth Factor (PlGF) proteins that are involved in the abnormal growth of new blood vessels. The abnormal growth of new blood vessels could leak blood and fluid, which causes disruption and dysfunction of the retina creating distortion and/or blind spots in central vision.

We are collaborating with Bayer HealthCare on the global development of EYLEA<sup>®</sup>. Bayer HealthCare has submitted applications for marketing authorization in the European Union, Japan, and other countries for wet AMD. Bayer HealthCare will market EYLEA<sup>®</sup> outside the United States, where the companies will share equally the profits from any future sales of EYLEA<sup>®</sup>. We maintain exclusive rights to EYLEA<sup>®</sup> in the United States and are entitled to all profits from any such sales.

##### ***ARCALYST*<sup>®</sup>    *CAPS***

Net product sales of ARCALYST<sup>®</sup> (rilonacept) in 2011 were \$19.9 million. Net product sales of ARCALYST<sup>®</sup> in 2010 were \$25.3 million, which included \$20.5 million of ARCALYST<sup>®</sup> net product sales made in 2010 and \$4.8 million of previously deferred net product sales, as described below under Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations - Results of Operations.

ARCALYST<sup>®</sup> is a protein-based product designed to bind the interleukin-1 (called IL-1) cytokine and prevent its interaction with cell surface receptors. ARCALYST<sup>®</sup> is available by prescription in the United States for the treatment of CAPS, including FCAS and MWS in adults and children 12 and older. CAPS are a group of rare, inherited, auto-inflammatory conditions characterized by life-long, recurrent symptoms of rash, fever/chills, joint pain, eye redness/pain, and fatigue. Intermittent, disruptive exacerbations or flares can be triggered at any time by exposure to cooling temperatures, stress, exercise, or other unknown stimuli.

**Clinical Programs:**

***1. EYLEA® Ophthalmologic Diseases***

We, together with our ex-U.S. collaborator Bayer HealthCare, are evaluating EYLEA® in Phase 3 programs in patients with central retinal vein occlusion (CRVO), diabetic macular edema (DME), and choroidal neovascularisation (CNV) of the retina as a result of pathologic myopia. We plan on initiating a Phase 3 study in branch retinal vein occlusion (BRVO) in the first quarter of 2012. Wet AMD, diabetic retinopathy (which includes DME), and retinal vein occlusion are three of the leading causes of adult blindness in the developed world. In these conditions, severe visual loss is caused by a combination of retinal edema and neovascular proliferation.

The Phase 3 trials in wet AMD, known as VIEW 1 and VIEW 2 (VEGF Trap: Interrogation of Efficacy and Safety in Wet age-related macular degeneration), compared EYLEA® and Lucentis® (ranibizumab injection), a registered trademark of Genentech, Inc. Lucentis® is an anti-VEGF agent approved for use and the current standard of care in wet AMD. VIEW 1 was conducted in North America and VIEW 2 was conducted in Europe, Asia Pacific, Japan, and Latin America. The VIEW 1 and VIEW 2 trials both evaluated EYLEA® doses of 0.5 milligrams (mg) and 2.0 mg at dosing intervals of four weeks and 2.0 mg at a dosing interval of eight weeks (following three initial monthly doses), compared with Lucentis® dosed according to its U.S. label, which specifies doses of 0.5 mg administered every four weeks over the first year. The primary endpoint of these non-inferiority studies was the proportion of patients treated with EYLEA® who maintain visual acuity at the end of one year compared to patients dosed monthly with Lucentis®. Visual acuity is defined as the total number of letters read correctly on the Early Treatment Diabetic Retinopathy Study (ETDRS) chart, a standard research tool for measuring visual acuity. Maintenance of vision is defined as losing fewer than three lines (equivalent to 15 letters) on the ETDRS chart. Secondary endpoints included the mean change from baseline in visual acuity as measured by ETDRS, the proportion of patients who gained at least 15 letters of vision at week 52, and the amount of fluid under the retina.

We and Bayer HealthCare announced week 52 results from the VIEW 1 and VIEW 2 studies in November 2010. In these studies, all regimens of EYLEA®, including EYLEA® dosed every two months, successfully met the primary endpoint of statistical non-inferiority compared to Lucentis® dosed every month. A generally favorable safety profile was observed for both EYLEA® and Lucentis®. The incidence of ocular treatment emergent adverse events was balanced across all four treatment groups in both studies, with the most frequent events associated with the injection procedure, the underlying disease, and/or the aging process. The most frequent ocular adverse events were conjunctival hemorrhage, macular degeneration, eye pain, retinal hemorrhage, and vitreous floaters. The most frequent serious non-ocular adverse events were typical of those reported in this elderly population who receive intravitreal treatment for wet AMD; the most frequently reported events were falls, pneumonia, myocardial infarction, atrial fibrillation, breast cancer, and acute coronary syndrome. There were no notable differences among the study arms.

Based on these positive results, we submitted a Biologics License Application (BLA) to the FDA in February 2011 for marketing approval of EYLEA® in wet AMD in the United States. In April 2011, the FDA accepted the BLA for filing and granted our request for Priority Review. In June 2011, the Dermatologic and Ophthalmic Drugs Advisory Committee of the FDA unanimously recommended that the FDA approve our BLA. In 2011, Bayer HealthCare submitted regulatory applications for marketing approval of EYLEA® in wet AMD in the European Union, Japan, and other countries. In November 2011, we received U.S. marketing approval from the FDA for EYLEA® Injection for the treatment of patients with wet AMD.

In December 2011, we and Bayer HealthCare announced Year 2 results from the VIEW 1 and VIEW 2 studies. In the second year of the studies, patients were treated with the same dose per injection as in the first year and were evaluated monthly to determine need for retreatment. Patients were treated at least every 12 weeks. All Year 2 analyses were considered exploratory. In an integrated analysis of the VIEW 1 and VIEW 2 studies, the visual acuity gain from baseline in the EYLEA® 2.0 mg every eight week group at week 96 was 7.6 letters compared to 8.4 letters at week 52, with an average of 11.2 injections over two years and 4.2 injections during the second year. The visual acuity gain from baseline in the monthly Lucentis® group at week 96 was 7.9 letters compared to 8.7 letters at week 52, with an average of 16.5 injections over two years and 4.7 injections during the second year. The results of each of the VIEW 1 and VIEW 2 studies were consistent with the integrated analysis.

The overall fewer average number of injections in the second year in the EYLEA® 2.0 mg every eight week group compared to the Lucentis® group (4.2 versus 4.7; nominal  $p < 0.0001$ ) was driven by the fact that fewer patients needed more intense therapy in the EYLEA® group and those patients required fewer injections.

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The proportion of patients who required frequent injections (six or more) during Year 2 was lower in the EYLEA<sup>®</sup> 2.0 mg every eight week group compared to the Lucentis<sup>®</sup> group (15.9% versus 26.5%). In the 25% of patients who required the most intense therapy (the greatest number of injections), patients in the EYLEA<sup>®</sup> 2.0 mg every eight week group required an average of 1.4 fewer injections in Year 2 compared to the Lucentis<sup>®</sup> group (6.6 versus 8.0). In the 25% of patients in each group who had the fewest number of injections in Year 2, the average number of injections was similar (approximately 3 for both groups, corresponding to the protocol-mandated minimum number of injections).

A generally favorable safety profile was observed for both EYLEA<sup>®</sup> and Lucentis<sup>®</sup>. The incidence of ocular treatment emergent adverse events was balanced across all four treatment groups in both studies. The most frequent ocular adverse events (greater than 10% of patients for the overall study population) were conjunctival hemorrhage, eye pain, retinal hemorrhage, and visual acuity reduced. The most frequent serious non-ocular adverse events were typical of those reported in this elderly population who receive intravitreal treatment for wet AMD; the most frequently reported events (greater than 1% of patients for the overall study population) were falls, pneumonia, myocardial infarction and atrial fibrillation. There were no notable differences among the study arms. The incidence of arterial thrombotic events as defined by the "Anti-Platelet Trialists" group criteria was 3.2% of patients for Lucentis<sup>®</sup> and 3.3% of patients in the combined EYLEA<sup>®</sup> groups.

In the fourth quarter of 2011, we and Bayer HealthCare initiated a Phase 3 trial, known as SIGHT, evaluating the efficacy and safety of EYLEA<sup>®</sup> in the neovascular form of wet AMD in China. EYLEA<sup>®</sup> will be evaluated for its effect on improving and maintaining vision when dosed as an intravitreal injection on a schedule of 2.0 mg every two months (following three initial monthly doses), as compared with Photodynamic Therapy (PDT) with verteporfin. After assessment of the primary endpoint at week 28, all patients, including those on PDT, will receive EYLEA<sup>®</sup> treatment until the end of the study at week 52. The trial will include approximately 300 patients and will be the largest retinal trial conducted in China. The SIGHT trial is being led by Bayer HealthCare.

EYLEA<sup>®</sup> was also in Phase 3 clinical studies for the treatment of CRVO, another cause of visual impairment. We led the COPERNICUS (COnrolled Phase 3 Evaluation of Repeated iNtravitreal administration of VEGF Trap-Eye In Central retinal vein occlusion: Uility and Safety) study, and Bayer HealthCare led the GALILEO (General Assessment Limiting Infiltration of Exudates in central retinal vein Occlusion with VEGF Trap-Eye) study. Patients in both studies received six monthly intravitreal injections of either EYLEA<sup>®</sup> at a dose of 2.0 mg or sham control injections. The primary endpoint of both studies was improvement in visual acuity versus baseline after six months of treatment as measured by the ETDRS eye chart. At the end of the initial six months, patients were dosed on an as-needed (PRN) basis for another six months. All patients were eligible for rescue laser treatment. In the COPERNICUS study, patients who were randomized to sham injections in the first six months were eligible to cross over to EYLEA<sup>®</sup> PRN dosing in the second six months.

In December 2010, we and Bayer HealthCare announced that in the COPERNICUS study, EYLEA<sup>®</sup> demonstrated a statistically significant improvement in visual acuity at six months compared to sham injections, the primary endpoint of the study. In this study, 56.1% of patients receiving EYLEA<sup>®</sup> gained at least 15 letters of vision from baseline, compared to 12.3% of patients receiving sham injections (p<0.0001). In the study, EYLEA<sup>®</sup> was generally well tolerated. The most common adverse events were those typically associated with intravitreal injections or the underlying disease. Serious ocular adverse events in the EYLEA<sup>®</sup> group were uncommon (3.5%), consisting of individual reports of corneal abrasion, endophthalmitis, retinal vein occlusion, and reduced visual acuity, and were more frequent in the control group (13.5%). The incidence of non-ocular serious adverse events was generally well-balanced between the treatment arms. There were no deaths among the 114 patients treated with EYLEA<sup>®</sup> and two (2.7%) in the 73 patients treated with sham injections.

The one-year COPERNICUS results showed that 55.3% of patients receiving EYLEA<sup>®</sup> dosed monthly for 24 weeks, then on a PRN basis (guided by anatomic and visual acuity monitoring) over the next 28 weeks, gained at least 15 letters from baseline on an ETDRS eye chart compared to 30.1% of patients who received sham injections for the first 24 weeks followed by EYLEA<sup>®</sup> PRN from week 24 to week 52 (p=0.0006). In terms of gain in visual acuity from baseline to week 52, patients receiving EYLEA<sup>®</sup> monthly for 24 weeks followed by EYLEA<sup>®</sup> PRN gained, on average, 16.2 letters of vision compared to a mean gain of 3.8 letters for patients who switched at week 24 from sham to EYLEA<sup>®</sup> PRN (p<0.0001). These results demonstrate that the benefits achieved with monthly EYLEA<sup>®</sup> treatment through week 24 were maintained out to week 52. At week 24, patients receiving EYLEA<sup>®</sup> had a mean gain of 17.3 letters, while patients receiving sham had a mean loss of 4.0 letters (p<0.0001). Patients who received EYLEA<sup>®</sup> monthly followed by EYLEA<sup>®</sup> PRN, were administered a mean of 2.7 EYLEA<sup>®</sup> injections from week 24 to 52, while patients who switched from sham to EYLEA<sup>®</sup> PRN received a mean of 3.9 EYLEA<sup>®</sup> injections. EYLEA<sup>®</sup> was generally well tolerated in the study. At week 52, the most frequently reported adverse events in patients who went from monthly EYLEA<sup>®</sup> to EYLEA<sup>®</sup> PRN were reduction of visual acuity, conjunctival hemorrhage, eye pain, and intraocular pressure increased. The most frequently reported adverse events in patients who switched from sham to EYLEA<sup>®</sup> PRN were reduction of visual acuity, conjunctival hemorrhage, intraocular pressure increased, and retinal hemorrhage. At week 52, 5.3% of patients receiving EYLEA<sup>®</sup> who switched to EYLEA<sup>®</sup> PRN and 16.2% of patients who switched from sham to EYLEA<sup>®</sup> PRN reported at least one ocular serious adverse event.

In April 2011, we and Bayer HealthCare announced that in the GALILEO study, EYLEA<sup>®</sup> also demonstrated a statistically significant improvement in visual acuity at six months compared to sham injections, the primary endpoint of the study. In this trial, 60.2% of patients receiving 2.0 mg of EYLEA<sup>®</sup> monthly gained at least 15 letters of vision from baseline, compared to 22.1% of patients receiving sham injections

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( $p < 0.0001$ ). Patients receiving 2.0 mg of EYLEA<sup>®</sup> monthly gained, on average, 18 letters of vision compared to a mean gain of 3.3 letters with sham injections ( $p < 0.0001$ ), a secondary endpoint.

As in the COPERNICUS trial, EYLEA<sup>®</sup> was generally well tolerated in the GALILEO study and the most common adverse events were those typically associated with intravitreal injections or the underlying disease. Serious ocular adverse events in the EYLEA<sup>®</sup> group were 2.9% and were more frequent in the control group (8.8%). The most frequently reported adverse events overall in the EYLEA<sup>®</sup> arm were eye pain, conjunctival hemorrhage, and elevated intraocular pressure. The most frequently reported adverse events in the control group were macular edema, eye irritation, and reduced visual acuity. The incidence of non-ocular serious adverse events was generally well-balanced between the treatment arms. The most frequent non-ocular adverse events were headache and nasopharyngitis. There were no deaths in the study.

The one-year GALILEO results showed that 60.2% of patients receiving EYLEA<sup>®</sup> dosed monthly for 24 weeks, then on a PRN basis (guided by anatomic and visual acuity monitoring) over the next 28 weeks, gained at least 15 letters from baseline on an ETDRS eye chart compared to 32.4% of patients receiving sham injections ( $p = 0.0004$ ). In terms of gain in visual acuity from baseline to week 52, patients receiving EYLEA<sup>®</sup> gained, on average, 16.9 letters of vision compared to a mean gain of 3.8 letters for patients receiving sham injections ( $p < 0.0001$ ). These results demonstrate that the benefits achieved with monthly EYLEA<sup>®</sup> treatment through week 24 were maintained out to week 52. At week 24, patients receiving EYLEA<sup>®</sup> had a mean gain of 18 letters compared to a mean gain of 3.3 letters for patients with sham injections ( $p < 0.0001$ ). Patients treated with EYLEA<sup>®</sup> received an average of 2.5 EYLEA<sup>®</sup> injections from week 24 to week 52. EYLEA<sup>®</sup> was generally well tolerated in the study. At week 52, the most frequently reported adverse events overall in the EYLEA<sup>®</sup> arm were macular edema, elevated intraocular pressure, eye pain, conjunctival hemorrhage, and retinal hemorrhage. The most frequently reported adverse events in the sham group were macular edema, retinal hemorrhage, retinal vascular disorder, reduction of visual acuity and eye irritation. At week 52, 9.6% of patients in the EYLEA<sup>®</sup> arm and 8.8% of patients in the sham arm presented with at least one ocular serious adverse event.



Based on the positive six-month results in the COPERNICUS and GALILEO studies, we submitted a supplemental BLA for U.S. regulatory approval of EYLEA® in CRVO in November 2011. Under the Prescription Drug User Fee Act (PDUFA), we were granted a target date for an FDA decision on our EYLEA® supplemental BLA of September 23, 2012. Bayer HealthCare plans to submit regulatory applications in this indication in Europe in late 2012 or early 2013.

In the second quarter of 2011, we and Bayer HealthCare initiated Phase 3 studies to evaluate the safety and efficacy of EYLEA® in DME. These clinical trials have three study arms. In the first arm, patients will be treated every month with 2.0 mg of EYLEA®. In the second arm, patients will be treated with 2.0 mg of EYLEA® every two months after an initial phase of monthly injections. In the third arm, the comparator arm, patients will be treated with macular laser photocoagulation. The primary endpoint of the study is mean change in visual acuity from baseline as measured by the ETDRS eye chart. All patients will be followed for three years. We are conducting one of these studies, called VISTA-DME (VEGF Trap-Eye: Investigation of Safety, Treatment effect, and Anatomic outcomes in DME), with study centers in the United States. Bayer HealthCare is conducting the second study, named VIVID-DME (VEGF Trap-Eye In Vision Impairment Due to DME), with study centers in Europe, Japan, and Australia. The VISTA-DME trial was fully enrolled in early 2012.

In the first quarter of 2011, we and Bayer HealthCare initiated a Phase 3 trial in Asia in collaboration with the Singapore Eye Research Institute (SERI) investigating the efficacy and safety of EYLEA® in patients with CNV of the retina as a result of pathologic myopia. The study, which will enroll approximately 110 patients, has started in Japan and is scheduled to run until June 2013.

In the first quarter of 2012, we plan to initiate a multinational study of EYLEA® in patients with BRVO (VIBRANT).

#### **Collaboration with Bayer HealthCare**

In October 2006, we entered into a license and collaboration agreement with Bayer HealthCare for the global development and commercialization outside the United States of EYLEA®. Under the agreement, we and Bayer HealthCare collaborate on, and share the costs of, the development of EYLEA® through an integrated global plan. Bayer HealthCare will market EYLEA® outside the United States, where the companies will share equally in profits from any future sales of EYLEA®. Commencing on the first commercial sale of EYLEA® in a major market country outside the United States, we will be obligated to reimburse Bayer HealthCare for 50% of the development costs that it has incurred under the agreement from our share of the collaboration profits. The reimbursement payment in any quarter will equal 5% of the then outstanding repayment obligation, but never more than our share of the collaboration profits in the quarter unless we elect to reimburse Bayer HealthCare at a faster rate. Within the United States, we retain exclusive commercialization rights to EYLEA® and are entitled to all profits from any such sales. We have received \$60 million in development milestone payments and can earn up to \$50 million in future milestone payments related to marketing approvals of EYLEA® in major market countries outside the United States. We can also earn up to \$135 million in sales milestone payments if total annual sales of EYLEA® outside the United States achieve certain specified levels starting at \$200 million.

#### **2. ZALTRAP® (aflibercept) also known as VEGF Trap Oncology**

ZALTRAP® (aflibercept) is a fusion protein that is designed to bind all forms of VEGF-A, VEGF-B, and PlGF, and prevent their interaction with cell surface receptors. VEGF-A (and to a lesser degree, PlGF) is required for the growth of new blood vessels (a process known as angiogenesis) that are needed for tumors to grow.

ZALTRAP® is being developed globally in cancer indications in collaboration with Sanofi. In April 2011, we and Sanofi announced that the Phase 3 VELOUR trial evaluating ZALTRAP® in combination with the FOLFIRI chemotherapy regimen [folinic acid (leucovorin), 5-fluorouracil, and irinotecan] versus a regimen of FOLFIRI plus placebo met its primary endpoint of improving overall survival (OS) in previously treated metastatic colorectal cancer (mCRC) patients. The VELOUR data were presented in June 2011 at the European Society of Medical Oncology World Congress on Gastrointestinal Cancer. In this study, the addition of ZALTRAP® to the FOLFIRI chemotherapy regimen significantly improved both overall survival (HR=0.817; p=0.0032) and progression-free survival (HR=0.758; p=0.00007) compared to FOLFIRI plus placebo. A similar effect was seen with ZALTRAP® therapy whether or not patients had received prior bevacizumab therapy.

In the VELOUR study, grade 3 or 4 adverse events that occurred with a more than two percent greater incidence in the ZALTRAP® arm than in the placebo arm included diarrhea, asthenia/fatigue, stomatitis/ulceration, infections, hypertension, GI/abdominal pains, neutropenia, neutropenic complications and proteinuria. Deaths on study treatment due to adverse events occurred in 2.4 percent of patients in the ZALTRAP® arm and in 1.0 percent of patients in the placebo arm.

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Based upon these positive findings, Sanofi submitted regulatory applications for marketing approval of ZALTRAP<sup>®</sup> for the treatment of previously-treated mCRC patients to the European Medicines Agency (EMA) in December 2011, and to the FDA in early February 2012.

Another randomized, double-blind Phase 3 trial (VENICE), which is fully enrolled, is evaluating ZALTRAP<sup>®</sup> as a first-line treatment for hormone-refractory metastatic prostate cancer in combination with docetaxel/prednisone. The VENICE trial is being monitored by an Independent Data Monitoring Committee (IDMC), a body of independent clinical and statistical experts. The IDMCs meet periodically to evaluate data from the trial and may recommend changes in study design or study discontinuation. In July 2011, the study's IDMC met for a scheduled interim analysis and recommended that the trial continue to completion. A final analysis will be conducted when a pre-specified number of events have occurred in this trial, which is anticipated in the second quarter of 2012.

In December 2011, we announced initial data from the Phase 2 AFFIRM study in the first-line mCRC setting of ZALTRAP<sup>®</sup> in combination with the modified FOLFOX6 [folinic acid (leucovorin), 5-fluorouracil, and oxaliplatin] chemotherapy regimen. The primary endpoint of the study was the Progression Free Survival (PFS) rate at one year. The results showed that in patients who received ZALTRAP<sup>®</sup>, the PFS rate at one year was similar to that seen in the standard therapy arm for patients who received modified FOLFOX6 alone. The study was not designed for a direct statistical comparison between arms. The control arm was used as an internal benchmark only. The side effect profile of ZALTRAP<sup>®</sup> was similar to what has been seen in prior trials with ZALTRAP<sup>®</sup>.

### **ZALTRAP<sup>®</sup> Collaboration with Sanofi**

We and Sanofi globally collaborate on the development and commercialization of ZALTRAP<sup>®</sup>. Under the terms of our September 2003 collaboration agreement, as amended, we and Sanofi will share co-promotion rights and profits on sales, if any, of ZALTRAP<sup>®</sup> outside of Japan for disease indications included in our collaboration. In Japan, we are entitled to a royalty of approximately 35% on annual sales of ZALTRAP<sup>®</sup>, subject to certain potential adjustments. We may also receive up to \$400 million in milestone payments upon receipt of specified marketing approvals, including up to \$360 million related to the receipt of marketing approvals for up to eight ZALTRAP<sup>®</sup> oncology and other indications in the United States or the European Union and up to \$40 million related to the receipt of marketing approvals for up to five oncology indications in Japan.

Under the ZALTRAP<sup>®</sup> collaboration agreement, as amended, agreed upon worldwide development expenses incurred by both companies during the term of the agreement will be funded by Sanofi. If the collaboration becomes profitable, we will be obligated to reimburse Sanofi out of our share of ZALTRAP<sup>®</sup> profits for 50% of the development expenses that they funded. The reimbursement payment in any quarter will equal 5% of the then outstanding repayment obligation, but never more than our share of the ZALTRAP<sup>®</sup> profits in the quarter unless we elect to reimburse Sanofi at a faster rate.

### **3. ARCALYST<sup>®</sup> (rilonacept) Inflammatory Diseases**

ARCALYST<sup>®</sup> is being developed for the prevention of gout flares in patients initiating uric acid-lowering therapy. Gout, a disease in which IL-1 may play an important role in pain and inflammation, is a very painful and common form of arthritis that results from high levels of uric acid, a bodily waste product normally excreted by the kidneys. The elevated uric acid can lead to formation of urate crystals in the joints of the toes, ankles, knees, wrists, fingers, and elbows. Uric acid-lowering therapy, most commonly allopurinol, is prescribed to eliminate the urate crystals and prevent them from reforming. Paradoxically, the initiation of uric acid-lowering therapy often triggers an increase in the frequency of gout attacks in the first several months of treatment, which may lead to discontinuation of therapy. The break-up of urate crystals can result in stimulation of inflammatory mediators, including IL-1, resulting in acute flares of joint pain and inflammation. These painful flares generally persist for at least five days.

We conducted a Phase 3 clinical development program with ARCALYST<sup>®</sup> in gout patients initiating uric acid-lowering therapy. The program consisted of three studies: PRE-SURGE 1 (PREvention Study against URate-lowering drug-induced Gout Exacerbations), PRE-SURGE 2, and RE-SURGE (REview of Safety Utilizing Rilonacept in Gout Exacerbations).

In June 2010, we announced that results from PRE-SURGE 1, a North America-based double-blind, placebo-controlled study, showed that ARCALYST<sup>®</sup> prevented gout attacks, as measured by the primary study endpoint of the number of gout flares per patient over the 16 week treatment period. In addition, all secondary endpoints of the study were positive (p<0.001 vs. placebo). Among these endpoints, treatment with ARCALYST<sup>®</sup> reduced the proportion of patients who experienced two or more flares during the study period by up to 88%. Treatment with ARCALYST<sup>®</sup> also reduced the proportion of patients who experienced at least one gout flare during the study period by up to 65%.



In February 2011, we reported the results of PRE-SURGE 2 and RE-SURGE. In the PRE-SURGE 2 efficacy study in gout patients initiating allopurinol therapy, which was identical to PRE-SURGE 1 in design and analysis, 248 patients were randomized. ARCALYST<sup>®</sup> met the primary and all secondary study endpoints. The primary endpoint was the number of gout flares per patient over the 16-week treatment period. Patients who received ARCALYST<sup>®</sup> at a weekly, self-administered, subcutaneous dose of either 160 mg or 80 mg had a 72% decrease in mean number of gout flares compared to the placebo group (p<0.0001). Among secondary endpoints, treatment with ARCALYST<sup>®</sup> reduced the proportion of patients who experienced two or more flares during the study period by up to 82%. In addition, treatment with ARCALYST<sup>®</sup> reduced the proportion of patients who experienced at least one gout flare during the study period by up to 63%.

We also announced that in the RE-SURGE study, which evaluated the safety of ARCALYST<sup>®</sup> versus placebo over 16 weeks, ARCALYST<sup>®</sup> was generally well tolerated, and the safety profile was consistent with that reported in the PRE-SURGE 1 and PRE-SURGE 2 studies. In the overall gout program, the most frequently reported adverse events were injection site reaction and headache.

In the RE-SURGE study, ARCALYST<sup>®</sup> also met all secondary endpoints, which evaluated efficacy, over the 16 week treatment period (p<0.0001). These included the number of gout flares per patient, the proportion of patients who experienced two or more flares, and the proportion of patients who experienced at least one gout flare during the study period.

Based on the results of the three Phase 3 studies, we submitted a supplemental BLA for U.S. regulatory approval of ARCALYST<sup>®</sup> for the prevention of gout flares in patients initiating uric acid-lowering therapy. In November 2011, the FDA accepted for review our supplemental BLA. Under PDUFA, we were granted a target date for an FDA decision on the ARCALYST<sup>®</sup> supplemental BLA of July 30, 2012.

We also initiated a long-term safety study in this setting, known as UPSURGE (Understanding long-term safety in a Preventative Study against Urate-lowering drug-induced Gout Exacerbations), during the fourth quarter of 2011.

We own worldwide rights to ARCALYST<sup>®</sup>.

#### **4. Sarilumab (REGN88; IL-6R Antibody) for inflammatory diseases**

IL-6 is a key cytokine involved in the pathogenesis of rheumatoid arthritis, causing inflammation and joint destruction. A therapeutic antibody to IL-6R, Actemra<sup>®</sup> (tocilizumab), a registered trademark of Chugai Seiyaku Kabushiki Kaisha, has been approved for the treatment of rheumatoid arthritis.

Sarilumab is a fully human monoclonal antibody to IL-6R generated using our *VelocImmune*<sup>®</sup> technology. In July 2011, we and Sanofi announced that in the Phase 2b stage of the MOBILITY trial in rheumatoid arthritis, patients treated with sarilumab in combination with a standard RA treatment, methotrexate (MTX), achieved a significant and clinically meaningful improvement in signs and symptoms of moderate-to-severe RA compared to patients treated with MTX alone. The Phase 2b stage of the MOBILITY study was a 306-patient, dose-ranging, multi-national, randomized, multi-arm, double-blind, placebo-controlled study, that compared five different dose regimens of sarilumab in combination with MTX to placebo plus MTX. The primary endpoint of the study was the proportion of patients achieving at least a 20% improvement in RA symptoms (ACR20) after 12 weeks.

In the Phase 2b stage of the MOBILITY trial, there was a dose response observed in patients receiving sarilumab in combination with MTX. An ACR20 response after 12 weeks was seen in 49.0% of patients receiving the lowest sarilumab dose regimen and 72.0% of patients receiving the highest dose regimen compared to 46.2% of patients receiving placebo and MTX (p=0.02, corrected for multiplicity, for the highest sarilumab dose regimen). The most common adverse events (>5%) reported more frequently in active treatment arms included infections (non-serious), neutropenia, and liver function test abnormalities. The types and frequencies of adverse events were consistent with those previously reported with IL-6 inhibition. The incidence of serious adverse events among the five sarilumab treatment groups and the placebo group was comparable.

Sarilumab also demonstrated significant benefit compared to placebo in secondary endpoints, including ACR 50, ACR 70, and Disease Activity Score (DAS) 28 scores, additional measures of clinical activity used in RA trials.

In July 2011, we and Sanofi announced that in the phase 2b ALIGN trial in ankylosing spondylitis (AS), sarilumab did not demonstrate significant improvements in the signs and symptoms of active AS compared to placebo in patients who had inadequate response to Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). Sarilumab was generally well tolerated. The most common adverse events reported more frequently in active treatment arms included infections and neutropenia.



During the third quarter of 2011, we and Sanofi initiated the Phase 3 stage of the Phase 2/3 MOBILITY study.

#### **5. REGN727 (PCSK9 Antibody) for LDL cholesterol reduction**

Elevated LDL cholesterol ( bad cholesterol ) level is a validated risk factor leading to cardiovascular disease. Statins are a class of drugs that lower LDL cholesterol by upregulating the expression of the LDL receptor (LDLR), which removes LDL from circulation. PCSK9 is a naturally occurring secreted protein that also modulates LDL cholesterol levels through its interaction with the LDL receptor. In a landmark study published in the *New England Journal of Medicine* in March 2006, patients with lower than normal PCSK9 levels due to a genetic abnormality not only had significantly lower levels of LDL cholesterol, but also a significant reduction in the risk of coronary heart disease. We used our *VelocImmune*<sup>®</sup> technology to generate a fully human monoclonal antibody inhibitor of PCSK9, called REGN727, that is intended to lower LDL cholesterol.

In May 2010, we announced that in an interim efficacy analysis of a dose-escalating, randomized, double-blind, placebo-controlled, Phase 1 trial in healthy volunteers, REGN727 achieved substantial, dose dependent decreases of LDL cholesterol. Each dosing cohort consisted of six treated and two placebo patients. In July 2010, we presented additional data from this Phase 1 program. At the highest intravenous dose tested, a single dose of REGN727 achieved a greater than 60% maximum mean reduction of LDL cholesterol from baseline that lasted for more than one month. At the highest subcutaneous dose tested, a single dose of REGN727 achieved a greater than 60% maximum mean reduction of LDL cholesterol from baseline that lasted for more than two weeks. In these early trials, REGN727 was generally safe and well tolerated with no trend in drug-related adverse events and no evidence of hepato- or myo-toxicity. Injection site reactions were minimal.

In July 2010, we also presented the results of an interim efficacy analysis of a dose escalating, randomized, double-blind, placebo-controlled Phase 1 trial of subcutaneously delivered REGN727 in hyperlipidemic patients (familial hypercholesterolemia and non-familial hypercholesterolemia) on stable doses of statins whose LDL levels were greater than 100 milligrams per deciliter (mg/dL). At the highest dose tested at that time, in eleven patients, a single dose of REGN727 achieved an approximately 40% maximum mean additional reduction of LDL cholesterol from baseline. No serious adverse events and no dose limiting toxicities were reported.

During 2011, three Phase 2 studies with subcutaneous regimens of REGN727 were initiated: (1) a randomized, double-blind, multi-dose, placebo controlled, 75-patient trial in patients with heterozygous familial hypercholesterolemia (heFH), (2) a randomized, double-blind, multi-dose, placebo controlled, 90-patient trial in combination with atorvastatin in patients with primary hypercholesterolemia, and (3) a randomized, double-blind, multi-dose, placebo controlled, 180-patient trial in combination with atorvastatin in patients with primary hypercholesterolemia and on stable doses of atorvastatin. The primary endpoint of each Phase 2 study is the change in LDL cholesterol from baseline compared to placebo over the study period.

In November 2011, we announced preliminary results from the Phase 2 heFH trial. The objective of the study was to compare the effect of adding REGN727 to the existing lipid lowering therapy in heFH patients. In the primary efficacy analysis of the study, after 12 weeks of treatment, patients who received different dosing regimens of REGN727 achieved mean LDL cholesterol reductions from baseline ranging from approximately 30% to greater than 65%, depending on the dosing regimen of REGN727, compared to a mean reduction of 10% with placebo ( $p < 0.05$  for all dose groups). Patients in the study are being followed for a total of 20 weeks for safety. In this trial, REGN727 was generally well tolerated over 12 weeks. There were no elevations in liver function tests greater than three times the upper limit of normal (ULN) and no cases of elevated creatine phosphokinase reported. The most common adverse event was injection site reaction and there were no serious adverse events on active treatment. Full safety data from the 8-week post-treatment monitoring period will be presented at a future medical congress upon final analysis.

In November 2011, we also announced preliminary results from the Phase 2 trial studying patients with primary hypercholesterolemia who were on stable doses of atorvastatin. The primary objective of the study was to compare the effect of switching to a high dose of atorvastatin alone (80mg) versus a high dose of atorvastatin combined with REGN727. In the primary endpoint of the study, after eight weeks of treatment, patients who received REGN727 plus atorvastatin 80mg achieved a greater than 65% reduction in mean LDL cholesterol compared to a mean reduction of 17% for atorvastatin 80mg alone ( $p < 0.001$ ). The study also included a third arm in which REGN727 was added to the stable low dose of atorvastatin and the patients achieved a greater than 65% reduction in mean LDL cholesterol. Patients in the study were followed for a total of 16 weeks for safety. In this trial, REGN727 was generally well tolerated over 16 weeks. There was one serious adverse event of dehydration in the REGN727 plus atorvastatin 80mg group that was deemed not treatment related. One patient in the REGN727 plus atorvastatin 80mg group with mildly elevated aspartate aminotransferase (AST) prior to randomization ( $>ULN$  and  $\leq 3ULN$ ) experienced an elevation of  $AST > 3ULN$  and  $\leq 5ULN$  and one patient discontinued therapy due to a hypersensitivity reaction (rash).

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Initial data from the third Phase 2 trial, studying subcutaneous regimens of REGN727 in combination with atorvastatin in patients with primary hypercholesterolemia, are expected to be available in the first half of 2012.

REGN727 is being developed in collaboration with Sanofi.

### **6. REGN668 (IL-4R Antibody) for allergic and immune conditions**

IL-4R is required for signaling by the cytokines IL-4 and IL-13. Both of these cytokines are critical mediators of immune response, which, in turn, drives the formation of Immunoglobulin E (IgE) antibodies and the development of allergic responses, as well as the atopic state that underlies asthma and atopic dermatitis.

REGN668 is a fully human monoclonal antibody generated using our *VelocImmune*<sup>®</sup> technology that is designed to bind to IL-4R. REGN668 is in a Phase 1b study in patients with atopic dermatitis and a Phase 2 study in eosinophilic asthma. REGN668 is being developed in collaboration with Sanofi.

### **7. REGN421 (Dil4 Antibody) for advanced malignancies**

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. VEGF was the first growth factor shown to be specific for blood vessels, by virtue of having its receptor primarily expressed on blood vessel cells. 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 Dil4, 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. Moreover, inhibition of tumor growth is enhanced by the combination of Dil4 and VEGF blockade in many preclinical tumor models.

REGN421 is a fully human monoclonal antibody to Dil4 generated using our *VelocImmune*<sup>®</sup> technology, and is in Phase 1 clinical development. REGN421 is being developed in collaboration with Sanofi.

### **8. REGN910 (ANG2 Antibody) for oncology**

In the fourth quarter of 2010, we initiated a Phase 1 study in an oncology setting of REGN910, an antibody that specifically blocks ANG2. The angiopoietins, which were discovered at Regeneron, are ligands for the endothelial cell receptor Tie2 and are essential for vascular development and angiogenesis. Unlike other family members, ANG2 is strongly upregulated by endothelial cells at sites of angiogenesis and vascular remodeling, including tumors.

REGN910 is a fully human monoclonal antibody generated using our *VelocImmune*<sup>®</sup> technology, which is being developed for cancer indications. REGN910 is being developed in collaboration with Sanofi.

### **9. REGN475 (NGF Antibody) for pain**

REGN475 is a fully human monoclonal antibody to NGF, generated using our *VelocImmune*<sup>®</sup> technology, which is designed to block pain sensitization in neurons. Preclinical experiments indicate that REGN475 specifically binds to and blocks NGF activity and does not bind to or block cell signaling for closely related neurotrophins such as NT-3, NT-4, or BDNF.

In May 2010, we announced positive results from an interim analysis of a randomized, double-blind, four-arm, placebo-controlled Phase 2 trial in 217 patients with osteoarthritis of the knee. In July 2010, we presented additional results from this trial through 16 weeks.

In December 2010, we were informed by the FDA that a case confirmed as avascular necrosis of a joint was seen in another company's anti-NGF program. The FDA believes this case, which follows previously-reported cases of joint replacements in patients on an anti-NGF drug candidate being developed by another pharmaceutical company, provides evidence to suggest a class-effect and has placed REGN475, along with the two other anti-NGF antibodies in development by competitors, on clinical hold. An FDA Arthritis Advisory Committee meeting is scheduled for March 12, 2012 to discuss possible safety issues related to anti-NGF compounds. There are currently no ongoing trials with REGN475.

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In February 2012, Sanofi elected not to continue co-development of REGN475, and Regeneron now has sole global rights to REGN475. Under the terms of our agreement, Sanofi remains obligated to fund agreed-upon REGN475 development costs through the end of 2012 and is entitled to receive a mid-single digit royalty on any future sales of REGN475.



#### **10. REGN728**

In the fourth quarter of 2010, clinical trials began with REGN728, a fully human monoclonal antibody generated using our *VelocImmune*<sup>®</sup> technology, against an undisclosed target. REGN728 is being developed in collaboration with Sanofi.

#### **11. REGN1033**

In December 2011, the FDA accepted our investigational new drug (IND) filing for REGN1033 and in January 2012, we initiated a Phase 1 clinical study. REGN1033 is a fully human monoclonal antibody generated using our *VelocImmune*<sup>®</sup> technology, against an undisclosed target. REGN1033 is being developed in collaboration with Sanofi.

#### **12. REGN846**

REGN846 is a fully human monoclonal antibody generated using our *VelocImmune*<sup>®</sup> technology, against an undisclosed target, and is being evaluated in a Phase 2a study in patients with atopic dermatitis. In July 2011, Sanofi elected not to continue co-development of REGN846, and Regeneron now has sole global rights to REGN846. Under the terms of our agreement, Sanofi remains obligated to fund REGN846 clinical costs through conclusion of a planned proof-of-concept trial and is entitled to receive a mid-single digit royalty on any future sales of REGN846.

#### **13. REGN1154**

REGN1154 is a fully human monoclonal antibody generated using our *VelocImmune*<sup>®</sup> technology, against an undisclosed target. In December 2011, we submitted a Phase 1 clinical trial protocol in Australia for REGN1154 under the clinical trial notification (CTN) regulatory process. We plan to initiate human studies in the first quarter of 2012 in Australia. Sanofi decided not to opt-in to the REGN1154 program and we have sole global rights. Under the terms of our agreement, Sanofi is entitled to receive a mid-single digit royalty on any future sales of REGN1154.

### **Research and Development Technologies:**

Many proteins that are either on the surface of or secreted by cells play important roles in biology and disease. 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 specific secreted proteins can have clinical benefit. In other cases, proteins on the cell-surface can mediate the interaction between cells, such as the processes that give rise to inflammation and autoimmunity.

Our scientists have developed two different technologies to design protein therapeutics to block the action of specific cell surface or secreted proteins. The first technology, termed the Trap technology, was used to generate our two approved products, ARCALYST<sup>®</sup> and EYLEA<sup>®</sup>, as well as ZALTRAP<sup>®</sup>, which is in Phase 3 clinical trials. 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. *VelociSuite*<sup>™</sup> is our second technology platform; it is used for discovering, developing, and producing fully human monoclonal antibodies that can address both secreted and cell-surface targets.

#### ***VelociSuite*<sup>™</sup>**

*VelociSuite*<sup>™</sup> consists of *VelocImmune*<sup>®</sup>, *VelociGene*<sup>®</sup>, *VelociMouse*<sup>®</sup>, and *VelociMab*<sup>®</sup>. The *VelocImmune*<sup>®</sup> mouse platform is utilized to produce fully human monoclonal antibodies. *VelocImmune*<sup>®</sup> was generated by exploiting our *VelociGene*<sup>®</sup> technology (see below), in a process in which six megabases of mouse immune gene loci were replaced, or humanized, with corresponding human immune gene loci. *VelocImmune*<sup>®</sup> mice can be used to generate efficiently fully human monoclonal antibodies to targets of therapeutic interest. *VelocImmune*<sup>®</sup> and our entire *VelociSuite*<sup>™</sup> 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*<sup>®</sup> technology to produce our next generation of drug candidates for preclinical and clinical development.

Our *VelociGene*<sup>®</sup> platform allows custom and precise manipulation of very large sequences of DNA to produce highly customized alterations of a specified target gene, or genes, 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 may be 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 preclinical development and pharmacology programs, *VelociGene*<sup>®</sup> offers the opportunity to humanize targets by replacing the mouse gene with the human homolog. Thus, *VelociGene*<sup>®</sup> 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.

Our *VelociMouse*<sup>®</sup> technology platform allows for the direct and immediate generation of genetically altered mice from embryonic stem cells (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. Furthermore, mice developed using our *VelociMouse*<sup>®</sup> technology are suitable for direct phenotyping or other studies. We have also developed our *VelociMab*<sup>®</sup> platform for the rapid screening of antibodies and rapid generation of expression cell lines for our Traps and our *VelocImmune*<sup>®</sup> human monoclonal antibodies.

### **Antibody Collaboration and License Agreements**

**Sanofi.** In November 2007, we and Sanofi entered into a global, strategic collaboration to discover, develop, and commercialize fully human monoclonal antibodies. The collaboration is governed by a Discovery and Preclinical Development Agreement and a License and Collaboration Agreement. In connection with the execution of the discovery agreement in 2007, we received a non-refundable, up-front payment of \$85.0 million from Sanofi. Pursuant to the collaboration, Sanofi is funding our research to identify and validate potential drug discovery targets and develop fully human monoclonal antibodies against these targets. We lead the design and conduct of research activities under the collaboration, including target identification and validation, antibody development, research and preclinical activities through filing of an Investigational New Drug Application (IND) or its equivalent, toxicology studies, and manufacture of preclinical and clinical supplies.

For each drug candidate identified through discovery research under the discovery agreement, Sanofi has the option to license rights to the candidate under the license agreement. If it elects to do so, Sanofi will co-develop the drug candidate with us through product approval. Development costs for the drug candidate are shared between the companies, with Sanofi generally funding these costs up front, except that following receipt of the first positive Phase 3 trial results for a co-developed drug candidate, subsequent Phase 3 trial-related costs for that drug candidate are shared 80% by Sanofi and 20% by us. We are generally responsible for reimbursing Sanofi for half of the total development costs for all collaboration antibody products from our share of profits from commercialization of collaboration products to the extent they are sufficient for this purpose. However, we are not required to apply more than 10% of our share of the profits from collaboration products in any calendar quarter towards reimbursing Sanofi for these development costs.

Sanofi will lead commercialization activities for products developed under the license agreement, subject to our right to co-promote such products. The parties will equally share profits and losses from sales within the United States. The parties will share profits outside the United States on a sliding scale based on sales starting at 65% (Sanofi)/35% (us) and ending at 55% (Sanofi)/45% (us), and will share losses outside the United States at 55% (Sanofi)/45% (us). In addition to profit sharing, we are entitled to receive up to \$250 million in sales milestone payments, with milestone payments commencing after aggregate annual sales outside the United States exceed \$1.0 billion on a rolling 12-month basis.

In November 2009, we and Sanofi amended these agreements to expand and extend our antibody collaboration. The goal of the expanded collaboration is to advance a total of 20 to 30 new antibody product candidates into clinical development from 2010 through 2017.

Under the amended discovery agreement, Sanofi agreed to fund up to \$160 million per year of our antibody discovery activities over the period from 2010-2017, subject to a one-time option for Sanofi to adjust the maximum reimbursement amount down to \$120 million per year commencing in 2014 if over the prior two years certain specified criteria were not satisfied. Sanofi has an option to extend the discovery program for up to an additional three years after 2017 for further antibody development and preclinical activities. Pursuant to the collaboration, Sanofi is also obligated to fund up to \$30 million of agreed-upon costs we incur to expand our manufacturing capacity at our Rensselaer, New York facilities.

In 2010, as we scaled up our capacity to conduct antibody discovery activities, Sanofi funded \$137.7 million of our preclinical research under the expanded collaboration. The balance between that amount and \$160 million, or \$22.3 million, has been added to the funding otherwise available to us in 2011-2012 under the amended discovery agreement.

From the collaboration's inception in November 2007 through December 31, 2011, Sanofi has funded a total of \$474.6 million of our costs under the discovery agreement and a total of \$400.4 million of our development costs under the license agreement, or a total of \$875.0 million in funding for our antibody research and development activities during this period.

In August 2008, we entered into an agreement with Sanofi to use our *VelociGene*<sup>®</sup> platform to supply Sanofi with genetically modified mammalian models of gene function and disease. Under this agreement, Sanofi is required to pay us a minimum of \$21.5 million for the term of the agreement, which extends through December 2012, for knock-out and transgenic models of gene function for target genes identified by Sanofi. Sanofi will use these models for its internal research programs that are outside of the scope of our antibody collaboration.

**Astellas Pharma Inc.** In March 2007, we entered into a six-year, non-exclusive license agreement with Astellas Pharma Inc. to allow Astellas to utilize our *VelocImmune*<sup>®</sup> technology in its internal research programs to discover human monoclonal antibodies. Under the terms of the agreement, Astellas made a \$20.0 million annual, non-refundable payment to us in each of the second quarters of 2007, 2008, 2009, and 2010. In July 2010, the license agreement with Astellas was amended and extended through June 2023. Under the terms of the amended agreement, Astellas made a \$165.0 million up-front payment to us in August 2010. In addition, Astellas will make a \$130.0 million second payment to us in June 2018 unless the license agreement has been terminated prior to that date. Astellas has the right to terminate the agreement at any time by providing 90 days advance written notice. Under certain limited circumstances, such as our material breach of the agreement, Astellas may terminate the agreement and receive a refund of a portion of its up-front payment or, if such termination occurs after June 2018, a portion of its second payment, to us under the July 2010 amendment to the agreement. We are entitled to receive a mid-single digit royalty on any future sales of antibody products discovered by Astellas using our *VelocImmune*<sup>®</sup> technology.

**AstraZeneca UK Limited.** In February 2007, we entered into a six-year, non-exclusive license agreement with AstraZeneca UK Limited to allow AstraZeneca to utilize our *VelocImmune*<sup>®</sup> technology in its internal research programs to discover human monoclonal antibodies. Under the terms of the agreement, AstraZeneca made a \$20.0 million annual, non-refundable payment to us in each of the first quarters of 2007, 2008, 2009, and 2010. In November 2010, as permitted by the agreement, MedImmune Limited (as successor by novation from AstraZeneca) gave written notice of voluntary termination of the agreement, effective in February 2011, thereby canceling its obligation to make either of the final two annual payments. We remain entitled to receive a mid-single digit royalty on any future sales of antibody products discovered by MedImmune using our *VelocImmune*<sup>®</sup> technology.

#### **Royalty Agreement with Novartis Pharma AG**

Under a June 2009 agreement with Novartis (that replaced a previous collaboration and license agreement), we receive royalties on worldwide sales of Novartis' canakinumab, a fully human anti-interleukin-IL1 antibody. The royalty rates in the agreement start at 4% and reach 15% when annual sales exceed \$1.5 billion. Canakinumab is marketed for the treatment of CAPS, has completed Phase 3 development for gout, and is in earlier stage development for atherosclerosis and other inflammatory diseases. We are unable to predict whether canakinumab will be approved for gout or any other indication in addition to CAPS, or whether, even if approved, canakinumab for such indication(s) will be successfully commercialized. Accordingly, we are unable to predict whether these royalties will ever contribute materially to our results of operations or financial condition. To date these royalties have been minimal.

#### **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 was to build a comprehensive and broadly available resource of knockout mice to accelerate the understanding of gene function and human diseases. Under the NIH grant, as amended, amounts received or receivable by us from the grant's inception through December 31, 2011 totaled \$25.1 million. No further funding will be received by us in connection with the NIH Grant.

#### **Research Programs**

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, cardiovascular diseases, and infectious diseases.

#### **Sales and Marketing**

We have a New Products Marketing and Planning group and a Market Research group to evaluate commercial opportunities for our targets and drug candidates, assess the competitive environment, and analyze the commercial potential of our product portfolio. This group works in close collaboration with our collaborators for co-developed products to develop marketing plans and forecasts and to develop and execute pre-launch market development programs.



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In connection with the sales and marketing of ARCALYST<sup>®</sup> for CAPS, we have a small marketing, trade, reimbursement, and distribution group to provide case management and reimbursement services to patients with CAPS and their treating physicians.

In preparation for the launch of EYLEA<sup>®</sup> for wet AMD in 2011, we hired and trained a full-service commercialization group to execute the launch of EYLEA<sup>®</sup>. The group includes experienced professionals in the fields of marketing, communications, professional education, patient education and advocacy, reimbursement and managed markets, trade and distribution, commercial operations, commercial analytics, market research, and forecasting. Moreover, we have hired, trained, and deployed a field-based organization of approximately 75 individuals, including regional sales directors, medical sales specialists, and reimbursement managers, each with 7+ years of experience in the biopharmaceutical industry in a variety of therapeutic areas including oncology, ophthalmology, immunology, and inflammation. We outsource the warehousing and distribution of our finished drug products.

### Manufacturing

Our manufacturing facilities are located in Rensselaer, New York and consist of three buildings totaling approximately 395,000 square feet of research, manufacturing, office, and warehouse space. We currently have approximately 54,000 liters of cell culture capacity at these facilities. At December 31, 2011, we employed 439 people at our Rensselaer facilities. There were no impairment losses associated with long-lived assets at these facilities as of December 31, 2011.

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 good manufacturing practice (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. We are approved to manufacture our marketed products at our Rensselaer facilities. If our manufacturing facilities fail to maintain compliance with FDA and other regulatory requirements, we may be required to suspend manufacturing. This would likely have a material adverse effect on our business, operating results, financial condition, and cash flows.

### Competition

We face substantial competition from pharmaceutical, biotechnology, and chemical companies (see Item 1A. Risk Factors Risks Related to Commercialization of EYLEA<sup>®</sup> for the Treatment of Wet AMD and Risks Related to Commercialization of Products ). Our competitors include Genentech (a member of the Roche group), Novartis, Pfizer Inc., Bayer HealthCare, Onyx Pharmaceuticals, Inc., Eli Lilly and Company, Abbott Laboratories, Sanofi, Merck & Co., Inc., Amgen Inc., AstraZeneca, Bristol-Myers Squibb, Johnson & Johnson, GlaxoSmithKline, 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. Competition from smaller competitors may also be or become more significant if those competitors acquire or discover patentable inventions, form collaborative arrangements, or merge with large pharmaceutical companies. Even if we are able to commercialize additional product candidates, one or more of our competitors may have brought a competitive product to market earlier than us or may have obtained or obtain patent protection that dominates or adversely affects our activities or products. Our ability to compete will depend, to a great extent, 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.

*EYLEA<sup>®</sup>*. The market for eye disease products is very competitive. Novartis and Genentech are collaborating on the commercialization and further development of a VEGF antibody fragment (Lucentis<sup>®</sup>) for the treatment of wet AMD, DME, RVO, and other eye indications. Lucentis<sup>®</sup> was approved by the FDA in June 2006 for the treatment of wet AMD and in June 2010 for the treatment of macular edema following retinal vein occlusion (RVO). Lucentis<sup>®</sup> was approved by the European Medicines Agency (EMA) for wet AMD in January 2007, for the treatment of DME in January 2011, and for the treatment of RVO in June 2011. Many other companies, including Genentech, are working on the development of product candidates and extended delivery devices for the potential treatment of wet AMD, DME, and RVO including those that act by blocking VEGF and VEGF receptors, as well as use of small interfering ribonucleic acids (siRNAs) that modulate gene expression. For example, in January, 2012, Genentech submitted an IND for an extended delivery device. In addition, ophthalmologists are using off-label, with success for the treatment of wet AMD, DME, and RVO, a third-party repackaged version of Genentech's approved VEGF antagonist, Avastin<sup>®</sup> (bevacizumab). The relatively low cost of therapy with Avastin<sup>®</sup> in patients with wet AMD presents a significant competitive challenge in this indication. The National Eye Institute (NEI) and others are conducting long-term, controlled clinical trials comparing Lucentis<sup>®</sup> to Avastin<sup>®</sup> in the treatment of wet AMD. One-year data from the Comparison of Age-Related Macular Degeneration Treatments Trial (CATT) were reported in April 2011 and indicated that Avastin<sup>®</sup> dosed monthly was non-inferior to Lucentis<sup>®</sup> dosed monthly in the primary efficacy endpoint of mean visual acuity gain at 52 weeks. Avastin<sup>®</sup> is also being evaluated in eye diseases in trials that have been initiated in the United Kingdom, Canada, Brazil, Mexico, Germany, Israel, and other areas. It may be difficult for EYLEA<sup>®</sup> to compete in this or other eye indications for which it may be

approved against Lucentis<sup>®</sup> and off-label use of Avastin<sup>®</sup> because doctors and patients have had significant experience using these medicines and because of the relatively low cost of Avastin<sup>®</sup>. Moreover, the recently reported results of the CATT study, combined with the relatively low cost of Avastin<sup>®</sup> in treating patients with wet AMD, may well exacerbate the competitive challenge which EYLEA<sup>®</sup> will face in this or other eye indications for which it may be approved. In addition, while we believe that ZALTRAP<sup>®</sup> would not be well tolerated if administered directly to the eye, if ZALTRAP<sup>®</sup> is approved for the treatment of certain cancers, there is a risk that third parties will attempt to repackage ZALTRAP<sup>®</sup> for off-label use and sale for the treatment of wet AMD and other diseases of the eye, which would present a potential low-cost competitive threat to EYLEA<sup>®</sup> for wet AMD or other eye indications.

*ARCALYST*<sup>®</sup>. In 2009, Novartis received regulatory approval in the United States and Europe for canakinumab, a fully human anti-interleukin-IL1 $\beta$  antibody, for the treatment of CAPS. In January 2011, Novartis announced that it had submitted an application to the EMA for approval of canakinumab in the treatment of gout flares. Novartis submitted a supplemental BLA to the FDA in the first quarter of 2011 for approval of canakinumab in gout, which was denied in August 2011 based upon safety concerns. Canakinumab is also in development for atherosclerosis and a number of other inflammatory diseases. In addition, there are both small molecules and antibodies in development by other third parties that are designed to block the synthesis of IL-1 or inhibit the signaling of IL-1. For example, Xoma Ltd., in collaboration with Servier, is developing an antibody to IL-1, and both Amgen and MedImmune are developing antibodies to the IL-1 receptor. These drug candidates could offer competitive advantages over *ARCALYST*<sup>®</sup>. The successful development and/or commercialization of these competing molecules could adversely affect sales of *ARCALYST*<sup>®</sup> for CAPS and delay or impair our ability to commercialize *ARCALYST*<sup>®</sup> for indications other than CAPS.

*ZALTRAP*<sup>®</sup>. Many companies are developing therapeutic molecules designed to block the actions of VEGF specifically and angiogenesis in general. A variety of approaches have been employed, including antibodies to VEGF, antibodies to the VEGF receptor, small molecule antagonists to the VEGF receptor tyrosine kinase, and other anti-angiogenesis strategies. Many of these alternative approaches may offer competitive advantages to aflibercept in efficacy, side-effect profile, durability of effect, or method of delivery. Additionally, some of these molecules are already approved for marketing and have a broader range of indications than our product candidate.

In particular, Genentech has an approved VEGF antagonist, Avastin<sup>®</sup>, on the market for treating certain cancers and a number of pharmaceutical and biotechnology companies are working to develop competing VEGF antagonists, including Novartis, Amgen, Imclone LLC/Eli Lilly, Pfizer, AstraZeneca, and GlaxoSmithKline. Many of these molecules are further along in development than *ZALTRAP*<sup>®</sup> and may offer competitive advantages over our molecule. Pfizer, Onyx (together with its partner Bayer HealthCare), and GlaxoSmithKline are selling and marketing oral medications that target tumor cell growth and new vasculature formation that fuels the growth of tumors.

*Monoclonal Antibodies*. Our clinical candidates in development are all fully human monoclonal antibodies which were generated using our *VelocImmune*<sup>®</sup> technology. Our antibody generation technologies and clinical candidates face competition from many pharmaceutical and biotechnology companies using various technologies.

Numerous other companies are developing therapeutic antibody products. Companies such as Pfizer, Johnson & Johnson, AstraZeneca, Amgen, Biogen Idec, Inc., Novartis, Genentech, Bristol-Myers Squibb, Abbott, and GlaxoSmithKline have generated therapeutic products that are currently in development or on the market that are derived from recombinant DNA that comprise human antibody sequences. As noted above, Astellas has licensed our *VelocImmune*<sup>®</sup> technology as part of their internal antibody development programs.

We are aware of several pharmaceutical and biotechnology companies actively engaged in the research and development of antibody products against targets that are also the targets of our early-stage product candidates. For example, Pfizer, Johnson & Johnson, and Abbott are developing antibody product candidates against NGF. Genentech is marketing an antibody against IL-6R (tocilizumab) for the treatment of rheumatoid arthritis and systemic juvenile idiopathic arthritis, and several other companies, including Centocor Ortho Biotech, Inc. and Bristol-Myers Squibb, have antibodies against IL-6 in clinical development for this disease. GlaxoSmithKline, in partnership with OncoMed Pharmaceuticals, Inc., has a Dll4 antibody in clinical development for the treatment of solid tumors. Aerovance has completed initial clinical trials of two formulations of a biologic directed against IL-4. Amgen previously had an antibody against IL-4R in clinical development for the treatment of asthma. Amgen and Pfizer have development programs for antibodies against PCSK9; Alnylam has a clinical program underway with an RNAi molecule against PCSK9. Amgen, Pfizer, and AstraZeneca have development programs underway for antibodies against ANG2.



*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 Roche, 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 any of these or other competitors 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, such developments may have an adverse effect on our business, operating results, financial condition, cash flows, or future prospects.

We also compete with academic institutions, governmental agencies, and other public or private research organizations, which conduct research, seek patent protection, and establish collaborative arrangements for the development and marketing of products that would provide royalties or other consideration for use of their technology. These institutions are becoming more active in seeking patent protection and licensing arrangements to collect royalties or other consideration for use of the technology 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 Item 1A. Risk Factors Risks Related to Intellectual Property and Market Exclusivity *We may be restricted in our development, manufacturing, 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, and the costs and expenses of ongoing patent litigation have been and will likely continue to be significant.* ). Our policy is to file patent applications to protect technology, inventions, and improvements that we consider important to our business and operations. As of December 31, 2011, we held an ownership interest in a total of approximately 186 issued patents in the United States and approximately 570 issued patents in foreign countries with respect to our products and technologies. In addition, we hold an ownership interest in hundreds of patent applications in the United States and foreign countries.

Our patent portfolio includes granted patents and pending patent applications covering our *VelociSuite* technologies, including our *VelocImmune*<sup>®</sup> mouse platform which produces fully human monoclonal antibodies. Our issued patents covering these technologies generally expire between 2020 and 2028. However, we continue to file patent applications directed to improvements to these technology platforms.

Our patent portfolio also includes issued patents and pending applications relating to our marketed products, ARCALYST<sup>®</sup> and EYLEA<sup>®</sup>, and our product candidates in clinical development. These patents cover the proteins and DNA encoding the proteins, manufacturing patents, method of use patents, and pharmaceutical compositions, as well as various methods of using the products. For each of ARCALYST<sup>®</sup>, EYLEA<sup>®</sup> and our late-stage product candidate, ZALTRAP<sup>®</sup>, these patents generally expire between 2020 and 2028. However, the projected patent terms may be subject to extension based on potential patent term extensions in countries where such extensions are available.

We also are the nonexclusive licensee of a number of additional patents and patent applications. In December 2011, we and Genentech entered into a Non-Exclusive License and Partial Settlement Agreement relating to ophthalmic sales of EYLEA<sup>®</sup> in the United States. Pursuant to this agreement, we received a non-exclusive license to certain patents relating to VEGF receptor proteins, known as the Davis-Smyth patents, and other technology patents. Under the terms of the agreement, we agreed to make payments to Genentech based on U.S. sales of EYLEA<sup>®</sup> commencing upon FDA approval of EYLEA<sup>®</sup> in November 2011 through May 7, 2016. We will be required to make a one-time, non-refundable \$60 million payment upon cumulative U.S. sales of EYLEA<sup>®</sup> reaching \$400 million. In addition, we agreed to pay royalties of 4.75% on cumulative U.S. sales of EYLEA<sup>®</sup> between \$400 million and \$3 billion and 5.5% on any cumulative U.S. sales of EYLEA<sup>®</sup> over \$3 billion.

In July 2008 we entered into an Amended and Restated Non-Exclusive License Agreement with Collectis S.A. pursuant to which we licensed certain patents and patent applications relating to a process for the specific replacement of a copy of a gene in the receiver genome by homologous recombination. Pursuant to this agreement, we agreed to pay Collectis a low, single-digit royalty based on any future revenue received by us from any future licenses or sales of our *VelociGene*<sup>®</sup> or *VelocImmune*<sup>®</sup> products or services. No royalties are payable to Collectis on any revenue from commercial sales of antibodies from our *VelocImmune*<sup>®</sup> technology, including antibodies developed under our

collaboration with Sanofi. We also have non-exclusive license agreements with Amgen and other organizations for patent rights related to ARCALYST®. In connection with these licenses, we pay a combined mid-single digit royalty on net sales of ARCALYST®.

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. The degree of patent protection that will be afforded to our products in the United States and other important commercial markets is uncertain and is dependent upon the scope of protection decided upon by the patent offices, courts, and governments in these countries. There is no certainty that our existing patents or others, if obtained, will provide us protection from competition or provide commercial benefit.

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 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 is expensive and time consuming, even if the outcome is favorable to us. It is possible that patents issued 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 (see Item 1A. Risk Factors - Risks Related to Intellectual Property and Market Exclusivity *We may be restricted in our development, manufacturing, 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, and the costs and expenses of ongoing patent litigation have been and will likely continue to be significant.* ).

### 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 ARCALYST<sup>®</sup>, EYLEA<sup>®</sup>, and our product candidates (see Item 1A. Risk Factors Risks Related to Commercialization of EYLEA<sup>®</sup> for Wet AMD - *Our regulatory approval for sales of EYLEA<sup>®</sup> is limited to the treatment of wet AMD and is limited to sales in the United States. If we don't receive approval for EYLEA<sup>®</sup> for other indications, or if approvals are not obtained for sales in other countries, our sales and profits will be limited* and Risks Related to the Development and Approval of Our Product Candidates and New Indications for Our Marketed Products *If we do not obtain regulatory approval for our product candidates or new indications for our marketed products, or maintain regulatory approval for EYLEA<sup>®</sup> in the United States, we will not be able to market or sell them, which would materially and negatively impact our business, results of operations, and prospects.* ). 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 IND, 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 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**

We manage our business as one segment which 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. This segment also includes revenues and expenses related to (i) research and development activities conducted under our collaboration agreements with third parties and our grant from the NIH, (ii) product sales, including EYLEA<sup>®</sup> for the treatment of wet AMD and ARCALYST<sup>®</sup> for the treatment of CAPS, (iii) licensing agreements to utilize our *VelocImmune*<sup>®</sup> technology, and (iv) the supply of specified, ordered research materials using our *VelociGene*<sup>®</sup> technology platform.

### **Employees**

As of December 31, 2011, we had 1,704 full-time employees, of whom 330 held a Ph.D. and/or M.D., or PharmD degree. 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 make available free of charge on or through our Internet website (<http://www.regeneron.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 Securities and Exchange Commission (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, prospects, operating results, and financial condition. The risks described below include forward-looking statements, and actual events and our actual results may differ materially from these forward-looking statements. Additional risks and uncertainties not currently known to us or that we currently deem immaterial may also impair our business, prospects, operating results, and financial condition. Furthermore, additional risks and uncertainties are described under other captions in this report and should also 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.*

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From inception on January 8, 1988 through December 31, 2011, we had a cumulative loss of \$1.3 billion. If we continue to incur operating losses and fail to become a profitable company, we may be unable to continue our operations. In the absence of substantial revenue from the sale of products, including our current sales of EYLEA<sup>®</sup>, and ARCALYST<sup>®</sup> or from other sources, the amount, timing, nature or source of which cannot be predicted, our substantial losses will continue as we conduct our research and development activities, commercialize our approved products, and prepare for possible commercialization of our other product candidates and new indications of our marketed products.

*We may 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 and new indications of our marketed products, continued commercialization of EYLEA® in the United States, to prepare for potential commercialization of our late-stage product candidates and new indications for our marketed products and, if one or more of those product candidates or additional indications receive(s) regulatory approval, to fund the launch of those product(s) or new indications. We believe our existing capital resources, together with funds generated by anticipated EYLEA® net product sales and funding we are entitled to receive under our collaboration agreements, will enable us to meet our anticipated operating needs; however, one or more of our collaboration agreements may terminate, our revenues may fall short of our projections or be delayed, or our expenses may increase, which could result in our capital being consumed significantly faster than anticipated. Our expenses may increase for many reasons, including expenses in connection with the launch and marketing of EYLEA® and the potential commercial launches of our late-stage product candidates and new indications for our marketed products, manufacturing scale-up, expenses related to clinical trials testing ARCALYST®, EYLEA®, REGN475, REGN846, or REGN1154, and expenses related to the potential requirement for us to fund 20% of Phase 3 clinical trial costs for any of our antibody product candidates being developed in collaboration with Sanofi.

We may require additional financing in the future and we may not be able to raise additional funds. If we are able to obtain additional financing through the sale of equity or convertible debt securities, such sales will likely be dilutive to our shareholders. Debt financing arrangements, if available given the current uncertainties in the global credit and financial markets, 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 be at interest rates and contain other terms that are not favorable to our shareholders. Should we require and be unable to (i) raise sufficient funds to complete the development of our product candidates, (ii) to successfully commercialize our late-stage product candidates or new indications for our marketed products if they obtain regulatory approval, and (iii) to continue our manufacturing and marketing of EYLEA® for the treatment of wet AMD, we may face delay, reduction, or elimination of our research and development or preclinical or clinical programs and our commercialization activities, which would significantly limit our potential to generate revenue. We cannot be certain how profitable, if at all, our current marketing of EYLEA® for the treatment of wet AMD will be and, even if we obtain regulatory approval for our product candidates or new indications for our marketed products, they may never be successfully launched or become profitable, in which case our business, prospects, operating results, and financial condition may be materially harmed.

*The value of our investment portfolio is influenced by varying economic and market conditions and may experience losses.*

As of December 31, 2011, our cash, cash equivalents, and marketable securities totaled \$810.6 million (including \$7.7 million of restricted cash and marketable securities). We have invested our excess cash primarily in direct obligations of the U.S. government and its agencies, other debt securities guaranteed by the U.S. government, and money market funds that invest in U.S. government securities. We consider assets classified as marketable securities to be available-for-sale, as defined by FASB authoritative guidance. Unrestricted and restricted marketable securities totaled \$325.2 million at December 31, 2011, are carried at fair value, and the unrealized gains and losses are included in other accumulated comprehensive income (loss) as a separate component of stockholders' equity. If the decline in the value of a security in our investment portfolio is deemed to be other-than-temporary, we write down the security to its current fair value and recognize a loss which may be fully charged against income. The current economic environment and the volatility of securities markets increase the risk that we may not recover the principal we invested and/or there may be further declines in the market value of securities in our investment portfolio. As a result, we may incur additional charges against income in future periods for other-than-temporary impairments or realized losses upon a security's sale or maturity, and such amounts may be material.

#### **Risks Related to the Development and Approval of Our Product Candidates and New Indications for Our Marketed Products**

*We believe that a significant portion of the value attributed to our company by investors is based on the commercial potential of EYLEA®. If approval for EYLEA® is not obtained in countries outside the United States, or approval is not obtained for other indications, or if we fail to maintain regulatory compliance and lose the marketing approval we have in the United States, or if the product is withdrawn for any reason, our business, prospects, operating results, and financial condition will be materially harmed.*

Whether EYLEA<sup>®</sup> is approved by regulatory authorities outside the United States or approved by the FDA for new indications, and the timing thereof, will depend on many factors, including the following:

- whether or not the FDA determines that the evidence gathered in well-controlled clinical trials, other clinical trials and nonclinical studies of EYLEA<sup>®</sup> demonstrates that it is safe and effective as a treatment for the indication under review; and
- whether or not the FDA is satisfied that the manufacturing facilities, processes, and controls for EYLEA<sup>®</sup> are adequate, that the labeling is satisfactory, and that plans for post-marketing studies, safety monitoring, and risk evaluation and management are sufficient;

In June 2011, Bayer HealthCare submitted regulatory applications for marketing approval of ELYEA<sup>®</sup> in wet AMD in the European Union and Japan. Analogous regulatory authorities in these and other countries outside the United States have similar discretion to the FDA as to approval of EYLEA<sup>®</sup> in those countries.

If Bayer HealthCare does not obtain approval to market EYLEA<sup>®</sup> in the European Union, Japan, or other countries, or if there are material delays in obtaining such approvals, our business, prospects, operating results, and financial condition will be materially harmed.

***If we do not obtain regulatory approval for our product candidates or new indications for our marketed products, or maintain regulatory approval for EYLEA<sup>®</sup> in the United States, we will not be able to market or sell them, which would materially and negatively impact our business, results of operations, and prospects.***

We cannot sell or market products without regulatory approval. If we do not obtain and maintain regulatory approval for our product candidates, including ARCALYST<sup>®</sup> for the treatment of diseases other than CAPS, EYLEA<sup>®</sup> for the treatment of ophthalmologic diseases other than wet AMD, and/or ZALTRAP<sup>®</sup> for one or more oncology indications, the value of our company, our results of operations, and our prospects will be materially harmed. Our product candidates, including ZALTRAP<sup>®</sup> for previously treated mCRC, EYLEA<sup>®</sup> for CRVO and DME, and ARCALYST<sup>®</sup> for the prevention of gout flares in patients initiating uric acid-lowering therapy, may not receive regulatory approval. If we are unable to obtain such approval(s), or if we are materially delayed in doing so, our business, prospects, results of operations, and financial condition will be materially harmed. In addition, if we fail to maintain regulatory approval for EYLEA<sup>®</sup> for the treatment of wet AMD, we may lose marketing approval and the ability to generate EYLEA<sup>®</sup> product sales revenue, which would materially and negatively impact our business, prospects, results of operations, and financial condition.

***Obtaining and maintaining regulatory approval for drug products is costly, time-consuming, and highly uncertain.***

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.

The FDA enforces Good Clinical Practices (GCPs) and other regulations through periodic inspections of trial sponsors, clinical research organizations (CROs), principal investigators, and trial sites. If we or any of the third parties conducting our clinical studies are determined to have failed to fully comply with GCPs, the study protocol or applicable regulations, the clinical data generated in those studies may be deemed unreliable. This could result in non-approval of our product candidates by the FDA, or we or the FDA may decide to conduct additional audits or require additional clinical studies, which would delay our development programs, require us to incur additional costs, and could substantially harm our business.

Before approving a new drug or biologic product, the FDA requires that the facilities at which the product will be manufactured or advanced through the supply chain be in compliance with current Good Manufacturing Practices, or cGMP, requirements and regulations governing the shipment and storage of the product. 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, labelers, or other parties performing steps in the supply chain are unable to maintain regulatory compliance, the FDA can impose regulatory sanctions, including, among other things, refusal to approve a pending application for a new drug or biologic product, or revocation of a pre-existing approval. As a result, our business, prospects, operating results, and financial condition may be materially harmed.





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, manufacturing, marketing and approval of drugs, and commercial sale and distribution of drugs in foreign countries. The foreign regulatory approval process and requirements include all of the risks associated with FDA approval as well as country specific regulations, and actions by a regulatory agency in a country or region with respect to a product candidate may have an impact on the approval process for that product candidate in another country or region. Whether or not we obtain FDA approval for a product in the United States, we must obtain approval of the product by the comparable regulatory authorities in foreign countries before we can conduct clinical trials of or market that product or any other product in those countries.

***Clinical trials required for our product candidates and new indications of our marketed products are expensive and time-consuming, and their outcome is highly uncertain. If any of our drug trials are delayed or yield unfavorable results, regulatory approval for our product candidates or new indications of our marketed products may be delayed or become unobtainable.***

As described above, we must conduct extensive testing of our product candidates and new indications of our marketed products 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, contractors, consultants, or trial subjects to comply with the trial plan, protocol, or applicable regulations related to GCPs. A clinical trial may fail because it did not include and retain 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.

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 that drug development program. The failure of clinical trials to demonstrate the safety and effectiveness of our clinical candidates for the desired indication(s) would preclude the successful development of those candidates for such indication(s), in which event our business, prospects, operating results, and financial condition may be materially harmed.

***Successful development of our current and future product candidates is uncertain.***

Only a small minority of all research and development programs ultimately result in commercially successful drugs. We are testing ZALTRAP<sup>®</sup> and EYLEA<sup>®</sup> in a number of late-stage clinical trials in various indications and ARCALYST<sup>®</sup> for the prevention of gout flares in patients initiating uric acid-lowering drug therapy. Clinical trials may not demonstrate statistically sufficient effectiveness and safety to obtain the requisite regulatory approvals for these product candidates in these indications. In a number of instances, we have terminated the development of product candidates due to a lack of or only modest effectiveness. Moreover, even if we obtain positive results from preclinical testing or clinical trials, we may not achieve the same success in future trials. Many companies in the biopharmaceutical industry, including our company, have suffered significant setbacks in clinical trials, even after promising results have been obtained in earlier trials.

In April 2011 we announced that our Phase 3 VELOUR trial of ZALTRAP<sup>®</sup> met its primary endpoint of improving overall survival in the treatment of patients with previously treated mCRC. Based upon these positive results, we and Sanofi submitted regulatory applications for marketing approval to the FDA and EMA. In January 2012, Roche announced that a Phase 3 trial of Avastin<sup>®</sup> (bevacizumab) had met the primary endpoint of overall survival in mCRC in patients who had previously received Avastin<sup>®</sup> with standard chemotherapy. The positive results of this trial in a similar patient population could impact the potential commercial opportunity for ZALTRAP<sup>®</sup> in mCRC. ZALTRAP<sup>®</sup> is also in a Phase 3 clinical trial in combination with a standard chemotherapy regimen for the treatment of first-line androgen independent prostate cancer. We do not have proof of concept data from early-stage, double-blind, controlled clinical trials that ZALTRAP<sup>®</sup> will be safe or effective in this cancer setting. In March 2010, Genentech announced that a Phase 3 trial of Avastin<sup>®</sup>, in combination with chemotherapy in men with prostate cancer, did not meet its primary endpoint. This trial had a very similar design to our ongoing Phase 3 trial of ZALTRAP<sup>®</sup> in prostate cancer.

We also reported positive Phase 3 trial results with EYLEA<sup>®</sup> in CRVO after six months of treatment and, based on these results, have submitted a supplemental BLA filing to the FDA for marketing approval in the United States of EYLEA<sup>®</sup> in CRVO. Under PDUFA, we were granted a target date for an FDA decision on our EYLEA<sup>®</sup> in CRVO supplemental BLA of September 23, 2012. However, this expected timing

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for an FDA decision may not be met, and the FDA may not grant such approval or such approval may be substantially delayed. The FDA could also require us to provide additional clinical data in connection with this application. There can be no assurance that we will receive regulatory approval for EYLEA® in CRVO.

We also reported positive results of a Phase 2 trial of EYLEA<sup>®</sup> for the treatment of DME and that we have initiated a Phase 3 program in that indication. A number of other potential new drugs and biologics which showed promising results in Phase 1 and 2 clinical trials subsequently failed to establish sufficient safety and efficacy data to obtain necessary regulatory approvals, and this could occur with respect to subsequent clinical trials of EYLEA<sup>®</sup> for the treatment of DME.

Based on the results of three Phase 3 studies, we have submitted a supplemental BLA filing to the FDA seeking approval of ARCALYST<sup>®</sup> for the prevention of gout flares in patients initiating uric acid-lowering drug therapy and, under PDUFA, we were granted a target date for an FDA decision on our ARCALYST<sup>®</sup> supplemental BLA of July 30, 2012. However, this expected timing for an FDA decision may not be met, and the FDA may not grant such approval or such approval may be substantially delayed. The FDA could also require us to provide additional clinical data in connection with this application. For example, in June 2011, following two positive Phase 3 trials, the Arthritis Advisory Committee of the FDA, voted to recommend against approval in a gout indication for Ilaris<sup>®</sup> (canakinumab), Novartis IL-1 inhibitor which works through a similar mechanism as ARCALYST<sup>®</sup> and, in August 2011, Novartis received a Complete Response letter from the FDA requesting additional information, including clinical data to evaluate the benefit-risk profile of Ilaris<sup>®</sup> in refractory patients.

Many of our clinical trials are conducted under the oversight of IDMCs. These independent oversight bodies are made up of external experts who review the progress of ongoing clinical trials, including available safety and efficacy data, and make recommendations concerning a trial's continuation, modification, or termination based on interim, unblinded data. Any of our ongoing clinical trials may be discontinued or amended in response to recommendations made by responsible IDMCs based on their review of such interim trial results. For example, in September 2009, a Phase 3 trial that was evaluating ZALTRAP<sup>®</sup> as a first-line treatment for metastatic pancreatic cancer in combination with gemcitabine was discontinued at the recommendation of an IDMC after a planned analysis of interim efficacy data determined that the trial would not meet its efficacy endpoint. The recommended termination of any of our ongoing late-stage clinical trials by an IDMC could negatively impact the future development of our product candidate(s), and our business may be materially harmed.

We are studying our antibody candidates in a wide variety of indications in clinical trials. Many of these trials are exploratory studies designed to evaluate the safety profile of these compounds and to identify what diseases and uses, if any, are best suited for these product candidates. These product candidates may not demonstrate the requisite efficacy and/or safety profile to support continued development for some or all of the indications that are being, or are planned to be, studied, which would diminish our clinical pipeline and could negatively affect our future prospects and the value of our company.

***Serious complications or side effects in connection with the use of our products and in clinical trials for our product candidates and new indications for our marketed products could cause our regulatory approvals to be revoked or limited or lead to delay or discontinuation of development of our product candidates or new indications for our marketed products, 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 and new indications for our marketed products. It is possible that as we test our drug candidates or new indications in larger, longer, and more extensive clinical programs, or as use of these drugs becomes more widespread if they receive regulatory approval, illnesses, injuries, and discomforts that were observed in earlier trials, as well as conditions that did not occur or went undetected in 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 or new indications for our marketed products has many side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or if the product candidate has received regulatory approval such approval may be revoked, which would severely harm our business.

ZALTRAP<sup>®</sup> is being studied for the potential treatment of certain types of cancer and EYLEA<sup>®</sup> is being studied in diseases of the eye in addition to wet AMD. There are many potential safety concerns associated with significant blockade of VEGF that may limit our ability to successfully develop ZALTRAP<sup>®</sup> and EYLEA<sup>®</sup> in each of the indications for which we are studying these product candidates. These serious and potentially life-threatening risks, based on clinical and preclinical experience of VEGF inhibitors, include bleeding, intestinal perforation, hypertension, proteinuria, congestive heart failure, heart attack, and stroke. In addition, patients given infusions of any protein, including ZALTRAP<sup>®</sup> 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 when large numbers of patients were treated. There are risks inherent in the intravitreal administration of drugs like EYLEA<sup>®</sup>, which can cause injury to the eye and other complications. For example, in our Phase 3 trials of EYLEA<sup>®</sup> in wet AMD, the most frequent ocular adverse events were conjunctival hemorrhage, macular degeneration, eye pain, retinal hemorrhage, and vitreous floaters. These and other complications or side effects could harm the development and/or commercialization of ZALTRAP<sup>®</sup> for the treatment of cancer or EYLEA<sup>®</sup> for the treatment of diseases of the eye.



As more patients begin to use ARCALYST<sup>®</sup> if it receives regulatory approval for the prevention of gout flares in patients initiating uric acid-lowering therapy, and to the extent it is tested in new disease settings, new risks and side effects associated with ARCALYST<sup>®</sup> may be discovered, and risks previously viewed as inconsequential could be determined to be significant. Like cytokine antagonists such as Ilaris<sup>®</sup> (canakinumab), a registered trademark of Novartis, Kineret<sup>®</sup> (anakinra) and Enbrel<sup>®</sup> (etanercept), registered trademarks of Amgen, and Remicade<sup>®</sup> (infliximab) a registered trademark of Centocor Ortho Biotech, ARCALYST<sup>®</sup> affects the immune defense system of the body by blocking some of its functions. Therefore, ARCALYST<sup>®</sup> may interfere with the body's ability to fight infections. As noted above, in June 2011, following two positive Phase 3 trials, the Arthritis Advisory Committee of the FDA voted to recommend against approval in a gout indication for Ilaris<sup>®</sup>, Novartis' IL-1 inhibitor which works through a similar mechanism as ARCALYST<sup>®</sup> and, in August 2011, Novartis received a Complete Response letter from the FDA requesting additional information, including clinical data to evaluate the benefit-risk profile of Ilaris<sup>®</sup> in refractory patients.

Treatment with Kineret<sup>®</sup>, a medication that works through the inhibition of IL-1, has been associated with an increased risk of serious infections, and serious, life threatening infections have been reported in patients taking ARCALYST<sup>®</sup>. These or other complications or side effects could cause regulatory authorities to revoke approvals of ARCALYST<sup>®</sup> for the treatment of CAPS or deny the approval of ARCALYST<sup>®</sup> for the prevention of gout flares in patients initiating uric acid-lowering treatment or other disease settings. Alternatively, we may be required to conduct additional clinical trials, make changes in the labeling of our product, or limit or abandon our efforts to develop ARCALYST<sup>®</sup> in new disease settings. Any such side effects may also result in a reduction, or even the elimination, of sales of ARCALYST<sup>®</sup> in the current or future approved indications.

We are studying REGN475, a fully human monoclonal antibody to NGF, in a variety of pain indications, including osteoarthritis of the knee. In December 2010, we were informed by the FDA that a case confirmed as avascular necrosis of a joint was seen in another company's anti-NGF program. The FDA believes this case, which follows previously-reported cases of joint replacements in patients on an anti-NGF drug candidate being developed by another pharmaceutical company, provides evidence to suggest a class-effect and placed REGN475 on clinical hold. The FDA Arthritis Advisory Committee is scheduled for March 12, 2012 to discuss possible safety issues related to anti-NGF compounds. There are currently no ongoing trials with REGN475 that are either enrolling or treating patients.

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

In addition to the safety, efficacy, manufacturing, and regulatory hurdles faced by our product candidates, the administration of recombinant proteins frequently causes an immune response, resulting in the creation of antibodies against the therapeutic protein. The antibodies can have no effect or can totally neutralize the effectiveness of the protein, or require that higher doses be used to obtain a therapeutic effect. In some cases, the antibody can cross react with the patient's own proteins, resulting in an auto-immune type disease. Whether antibodies will be created can often not be predicted from preclinical or clinical experiments, and their detection or appearance is often delayed, so neutralizing antibodies may be detected at a later date, in some cases even after pivotal clinical trials have been completed.

***We may be unable to formulate or manufacture our product candidates in a way that is suitable for clinical or commercial use, which would delay or prevent continued development of such candidates and/or receipt of regulatory approval or commercial sale, which could materially harm our business.***

If we are unable to continue to develop suitable product formulations or manufacturing processes to support large scale clinical testing of our product candidates, including our antibody candidates, we may be unable to supply necessary materials for our clinical trials, which would delay or prevent the development of our product candidates. Similarly, if we are unable, directly or through our collaborators or third parties, to supply sufficient quantities of our products or develop formulations of our product candidates suitable for commercial use, we will be unable to obtain regulatory approval for those product candidates.

#### **Risks Related to Commercialization of EYLEA<sup>®</sup> for the Treatment of Wet AMD**

***We are subject to significant ongoing regulatory obligations and oversight with respect to EYLEA<sup>®</sup> for the treatment of wet AMD. If we fail to maintain regulatory compliance for EYLEA<sup>®</sup>, we may lose marketing approval, which would materially harm our business, prospects, operating results, and financial condition.***

EYLEA<sup>®</sup> is currently approved for treatment of wet AMD in the United States and Bayer HealthCare is seeking approval in other countries. We are subject to significant ongoing regulatory obligations with respect to EYLEA<sup>®</sup> for the treatment of wet AMD in the United States, and, if approved outside the United States, commercialization of EYLEA<sup>®</sup> will be subject to significant ongoing regulatory obligations and oversight in those countries where approval is obtained as well. If we fail to maintain regulatory compliance for EYLEA<sup>®</sup> for the treatment of wet AMD, we may lose marketing approval, which would materially harm our business, prospects, operating results, and financial condition. Failure to comply may also subject us to sanctions, product recalls, or withdrawals of previously approved marketing applications. See also *If we fail to meet the stringent requirements of governmental regulation in the manufacture of drug products or product candidates, we could incur substantial remedial costs, delays in the development or approval of our product candidates and/or in their commercial launch if they obtain regulatory approval, and a reduction in sales.*

***Serious complications or side effects in connection with the use of EYLEA<sup>®</sup> could materially harm our business, prospects, operating results, and financial condition.***

There are risks inherent in intravitreal injections, including with EYLEA<sup>®</sup>, such as intraocular inflammation, sterile and culture positive endophthalmitis, corneal decomposition, retinal detachment, retinal tear, and other side effects, all of which are reported from time to time to the FDA. Serious complications or serious, unexpected side effects in connection with the use of EYLEA<sup>®</sup> could materially harm our business, prospects, operating results, and financial condition.

***Our regulatory approval for sales of EYLEA<sup>®</sup> is limited to the treatment of wet AMD and is limited to sales in the United States. If we don't receive approval for EYLEA<sup>®</sup> for other indications, or if approvals are not obtained for sales in other countries, sales and profits will be limited.***

We have received regulatory approval for sale of EYLEA<sup>®</sup> for the treatment of wet AMD only in the United States. If we do not receive approval for EYLEA<sup>®</sup> for other uses, or if approvals for sales in other countries are not obtained, sales will be limited and our potential for profits will be limited. As a result, our business, prospects, results of operations, and financial condition would be materially impacted.

***Our sales of EYLEA<sup>®</sup> for the treatment of wet AMD are dependent on the availability and extent of reimbursement from third party payers, and changes to such reimbursement may materially harm our sales and potential revenue and harm our business, prospects, operating results, and financial condition.***

Our current sales in the United States of EYLEA<sup>®</sup> for the treatment of wet AMD are dependent, in part, on the availability and extent of reimbursement from third-party payers, including government programs such as Medicare and Medicaid and private payer healthcare and insurance programs. If approved for sale in other countries, such sales will be dependent, in part, on similar programs in these countries. In the United States, there is an increased focus from the federal government and others on analyzing the impact of various regulatory programs on the federal deficit, which could result in increased pressure on federal programs to reduce costs, including limiting federal healthcare expenditures. Economic pressure on state budgets may also have a similar impact. A reduction in the availability or extent of reimbursement from U.S. government programs could have a material adverse effect on the sales of EYLEA<sup>®</sup>. Since EYLEA<sup>®</sup> for the treatment of wet AMD is too expensive for most patients to afford without health insurance coverage, if adequate coverage and reimbursement by third-party payers, including Medicare and Medicaid in the United States, is not available, our ability to successfully commercialize EYLEA<sup>®</sup> will be materially adversely impacted. Our sales and potential profits and our business, prospects, operating results, and financial condition would be materially harmed. See also *"The successful commercialization of EYLEA<sup>®</sup> for the treatment of wet AMD as well as our late-stage product candidates or new indications for our marketed products, if approved, will depend on obtaining coverage and reimbursement for use of these products from third-party payers, including Medicare and Medicaid in the United States, and these payers may not agree to cover or adequately reimburse for use of our products or may do so at levels that make our products uncompetitive and/or unprofitable, which would materially harm our business, prospects, operating results, and financial condition."*

The status of a J-code for EYLEA<sup>®</sup> could also affect reimbursement. J-codes are permanent reimbursement codes maintained by Centers for Medicare and Medicaid Services (CMS) that are a component of the Healthcare Common Procedure Coding System (HCPCS), and are typically used to report injectable drugs that ordinarily cannot be self-administered. We do not currently have a J-Code for EYLEA<sup>®</sup>, although we anticipate assignment of a J-Code for EYLEA<sup>®</sup> in January 2013. Without a unique J-code identifier, EYLEA<sup>®</sup> must be billed using a non-specific miscellaneous J-code. Since such codes may be used for a wide variety of products, health plans may have more difficulty determining the actual product used and billed for the patient. As a result, these claims must often be submitted with additional information and manually processed, which can create delays in claims processing times as well as increasing the likelihood for claim errors.



***The commercial success of EYLEA® currently being marketed for the treatment of wet AMD is subject to strong competition.***

The market for eye disease products is very competitive. Novartis and Genentech are collaborating on the commercialization and further development of a VEGF antibody fragment, Lucentis® for the treatment of wet AMD, CRVO, DME, and other eye indications. Lucentis® was approved by the FDA in June 2006 for the treatment of wet AMD and in June 2010 for the treatment of macular edema following retinal vein occlusion (RVO), CRVO, and branch retinal vein occlusion (BRVO). Lucentis® was also approved by the EMA for wet AMD in January 2007 and for DME in January 2011. Many other companies are working on the development of product candidates for the potential treatment of wet AMD and DME including those that act by blocking VEGF and VEGF receptors, as well as small interfering ribonucleic acids (siRNAs) that modulate gene expression. In addition, ophthalmologists are using off-label, with success for the treatment of wet AMD, DME, and RVO, third-party repackaged versions of Genentech's approved VEGF antagonist, Avastin®. The relatively low cost of therapy with Avastin® in patients with wet AMD presents a significant competitive challenge in this indication.

The National Eye Institute (NEI) and others are conducting long-term, controlled clinical trials comparing Lucentis® to Avastin® in the treatment of wet AMD. One-year data from the CATT were reported in April 2011 and indicated that Avastin® dosed monthly was non-inferior to Lucentis® dosed monthly in the primary efficacy endpoint of mean visual acuity gain at 52 weeks. Avastin® is also being evaluated in eye diseases in trials that have been initiated in the United Kingdom, Canada, Brazil, Mexico, Germany, Israel, and other countries. It may be difficult for EYLEA® in this or other eye indications for which it may be approved to compete against Lucentis® and off-label use of Avastin® because doctors and patients have had significant experience using these medicines. Moreover, the recently reported results of the CATT study, combined with the relatively low cost of Avastin® in treating patients with wet AMD, may well exacerbate the competitive challenge which EYLEA® will face in this or other eye indications for which it may be approved. In addition, while we believe that ZALTRAP® would not be well tolerated if administered directly to the eye, if ZALTRAP® is approved for the treatment of certain cancers, there is a risk that third parties will attempt to repackage ZALTRAP® for off-label use and sale for the treatment of wet AMD and other diseases of the eye, which would present a potential low-cost competitive threat to EYLEA® for wet AMD or other eye indications. See also *The commercial success of EYLEA® currently being marketed for the treatment of wet AMD, and for our other product candidates or new indications for our marketed products, if any are approved for marketing, is highly uncertain given their method of administration, and because our competitors have received approval for and may be marketing products with a similar mechanism of action or may enter the marketplace with better or lower cost drugs.*

#### **Risks Related to Intellectual Property and Market Exclusivity**

***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 disclosed, by our own employees, our collaborators or otherwise, 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, including our company, 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 pending patent applications in the European Patent Office and it is likely that we will need to defend patent applications from third-party challengers from time to time in the future. Patent applications filed in the United States may also be challenged by third parties who file a request for post-grant review under the America Invents Act of 2011, beginning on September 16, 2012. We expect that post-grant review proceedings will become common in the United States and will be costly to defend. We have pending patent applications in the United States Patent and Trademark Office and it is likely that we will need to defend patent applications from third-party challengers from time to time in the future. Our patent rights may not provide us with a proprietary position or competitive advantages against competitors. Furthermore, even if the outcome is favorable to us, the enforcement of our intellectual property rights can be extremely expensive and time consuming.

***We may be restricted in our development, manufacturing, 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, and the costs and expenses of ongoing patent litigation have been and will likely continue to be significant.***



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 or even to products that have received regulatory approval and are being or have been commercialized, 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*<sup>®</sup> technology, either because of the way the antibodies are discovered or produced or because of a proprietary composition covering an antibody or the antibody's target.

We are aware of issued patents and pending patent applications owned by Genentech that claim certain chimeric VEGF receptors. We do not believe that ZALTRAP<sup>®</sup> or EYLEA<sup>®</sup> infringe any valid claim in these patents or patent applications. We are involved in five patent litigations with Genentech, two in the United States and three in Europe. In November 2010, we commenced a lawsuit against Genentech in the U.S. District Court for the Southern District of New York (the Court), seeking a declaratory judgment that no activities relating to our VEGF Trap infringe any valid claim of certain Genentech patents referred to as the Davis-Smyth patents (the First Davis-Smyth Case). Genentech answered the complaint and asserted counterclaims that our prior or planned activities relating to VEGF Trap have infringed or will infringe claims of four of the five Davis-Smyth patents and requested a judgment against us for damages, including for willful infringement, and other relief as the Court deems appropriate.

On December 31, 2011, we entered into a non-exclusive license and partial settlement agreement (the Agreement) with Genentech that covers making, using, and selling EYLEA<sup>®</sup> in the United States for the prevention and treatment of human eye diseases and disorders in the United States. Under the Agreement, we received a non-exclusive license to the Davis-Smyth patents, and certain other technology patents owned or co-owned by Genentech. The Agreement does not cover any non-U.S. patent rights or non-U.S. patent disputes, and does not cover any use of aflibercept other than for prevention and treatment of human eye diseases and disorders in the United States. The First Davis-Smyth Case is continuing with respect to matters not covered by the Agreement. The Agreement provides for us to make payments to Genentech based on U.S. sales of EYLEA<sup>®</sup> through May 7, 2016, the date the Davis-Smyth patents expire. We will make a lump-sum payment of \$60 million once cumulative U.S. sales of EYLEA<sup>®</sup> reach \$400 million. We will also pay royalties of 4.75% on cumulative U.S. sales of EYLEA<sup>®</sup> between \$400 million and \$3 billion and 5.5% on any cumulative U.S. sales of EYLEA<sup>®</sup> over \$3 billion. As a result of the Agreement, on January 17, 2012 Genentech filed a second amended answer and counterclaim in the First Davis-Smyth Case, in which it amended its counterclaims alleging infringement of four of the five Davis-Smyth patents. On December 23, 2011, Genentech initiated a related case in the Court against Regeneron and Sanofi alleging infringement of four of the five Davis-Smyth Patents by activities relating to VEGF Trap (but excluding EYLEA<sup>®</sup>) (the Second Davis-Smyth Case). As in the First Davis-Smyth Case, in the new complaint Genentech requests a judgment against us for damages, including for willful infringement, and other relief as the Court deems appropriate.

We believe Genentech's claims in the First Davis Smyth Case and the Second Davis Smyth Case are without merit and intend to continue to defend against all of Genentech's remaining claims vigorously. However, it is possible that there could be an adverse determination or judgment in either or both cases that would materially harm our business by requiring us to seek a license for matters not covered by the Agreement, which may not be available at all or on reasonable terms, or precluding the manufacture, further development, or sale of EYLEA<sup>®</sup> outside the United States or ZALTRAP<sup>®</sup>, or resulting in a damage award. In addition, irrespective of the outcome of the Davis-Smyth cases, we have incurred and will likely continue to incur significant costs and expenses associated with them, which have negatively affected, and will likely continue to negatively affect, our results of operations. An adverse determination in any of the proceedings described herein may have a material adverse effect on our business, prospects, results of operations, and financial condition.

We have initiated patent-related actions against Genentech in Germany, the United Kingdom, and Italy, and may initiate other actions in other countries outside the United States, which could have similar or other adverse outcomes that would materially harm our business and which, irrespective of the outcomes, may also entail significant costs and expenses.

We are aware of patents and pending applications owned by Roche that claim antibodies to IL-6R and methods of treating rheumatoid arthritis with such antibodies. We are developing sarilumab, an antibody to IL-6R, for the treatment of rheumatoid arthritis. Although we do not believe that sarilumab infringes any valid claim in these patents or patent applications, Roche could initiate a lawsuit for patent infringement and assert its patents are valid and cover sarilumab.

We are aware of a U.S. patent jointly owned by Genentech and City of Hope relating to the production of recombinant antibodies in host cells. We currently produce our antibody product candidates using recombinant antibodies from host cells and may choose to produce additional antibody product candidates in this manner. Neither ARCALYST<sup>®</sup>, ZALTRAP<sup>®</sup>, nor EYLEA<sup>®</sup> are recombinant antibodies. If any of our antibody product candidates are produced in a manner subject to valid claims in the Genentech patent, then we may need to obtain a license from Genentech, should one be available. Genentech has licensed this patent to several different companies under confidential license agreements. If we desire a license for any of our antibody product candidates and are unable to obtain a license on commercially reasonable terms or at all, we may be restricted in our ability to use Genentech's techniques to make recombinant antibodies in or to import them into the United States.

Further, we are aware of a number of other third-party patent applications that, if granted with claims as currently drafted, may cover our current or planned activities. It could be determined that our products and/or actions in manufacturing or selling our product candidates infringe such patents.

Patent holders in addition to Genentech could assert claims against 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 drug candidates, including EYLEA<sup>®</sup> or our other late-stage product 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 those drugs and may be required to pay costly damages. Such a result may materially harm our business, prospects, operating results, and financial condition. In any event, 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 or advisable. 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.

***Loss or limitation of patent rights, and new regulatory pathways for biosimilar competition, could reduce the duration of market exclusivity for our products.***

In the pharmaceutical and biotechnology industries, the majority of an innovative product's commercial value is usually realized during the period in which it has market exclusivity. In the United States and some other countries, when market exclusivity expires and generic versions of a product are approved and marketed, there usually are very substantial and rapid declines in the product's sales.

If our late-stage product candidates or other clinical candidates are approved for marketing in the U.S or elsewhere, market exclusivity for those products will generally be based upon patent rights and/or certain regulatory forms of exclusivity. As described above under "*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*", the scope and enforceability of our patent rights may vary from country to country. The failure to obtain patent and other intellectual property rights, or limitations on the use, or the loss, of such rights could be material to us. Absent patent protection or regulatory exclusivity for our products, it is possible, both in the United States and elsewhere, that generic and/or biosimilar versions of those products may be approved and marketed which would likely result in substantial and rapid reductions in revenues from sales of those products.

Under the federal Patient Protection and Affordable Care Act, or PPACA, enacted in 2010, there is now a new, abbreviated path in the United States for regulatory approval of biosimilar versions of biological products. The PPACA provides a regulatory mechanism that allows for FDA approval of biologic drugs that are similar to (but not generic copies of) innovative drugs on the basis of less extensive data than is required by a full BLA. Under this new regulation, an application for approval of a biosimilar may be filed four years after approval of the innovator product. However, qualified innovative biological products will receive 12 years of regulatory exclusivity, meaning that the FDA may not approve a biosimilar version until 12 years after the innovative biological product was first approved by the FDA. However, the term of regulatory exclusivity may not remain at 12 years in the United States and could be shortened.

The increased likelihood of biosimilar competition has increased the risk of loss of innovators' market exclusivity. Due to this risk, and uncertainties regarding patent protection, if our late-stage product candidates or other clinical candidates are approved for marketing, it is not possible to predict the length of market exclusivity for a particular product with certainty based solely on the expiration of the relevant patent(s) or the current forms of regulatory exclusivity. It is also not possible to predict changes in United States regulatory law that might reduce biological product regulatory exclusivity. The loss of market exclusivity for a product would likely materially and negatively affect revenues from product sales of that product and thus our financial results and condition.

### **Risks Related to Manufacturing and Supply**

***We rely on limited internal and contracted manufacturing and supply chain capacity, which could result in our being unable to continue to successfully commercialize EYLEA<sup>®</sup> and to commercialize our other product candidates or other indications for our marketed products if they receive regulatory approval and are unable to continue to develop our clinical candidates.***

Our manufacturing facility would be inadequate to produce the active pharmaceutical ingredients of (a) EYLEA<sup>®</sup>, ZALTRAP<sup>®</sup>, and ARCALYST<sup>®</sup> for the treatment of gout flares in sufficient commercial quantities if these late-stage product candidates were all to receive regulatory approval, and (b) our earlier stage product candidates in sufficient clinical quantities if our clinical pipeline advances as planned. In addition to expanding our internal capacity, we intend to rely on our corporate collaborators, as well as contract manufacturers, to produce commercial quantities of drug material needed for commercialization of our products to the extent such quantities are not manufactured at our own facility. We rely entirely on third-parties and our collaborators for filling and finishing services. Generally, in order for other parties to perform any step in the manufacturing and supply chain, we must transfer technology to the other party which can be time consuming and may not be successfully accomplished without considerable cost and expense, or at all. We will have to depend on these other parties to perform effectively on a timely basis and to comply with regulatory requirements. If for any reason they are unable to do so, and as a result we are unable to directly or through such third parties manufacture and supply sufficient commercial quantities of our products on acceptable terms, or if we should encounter delays or other difficulties in our relationships with our corporate collaborators, third-party manufacturers, or other parties involved in our supply chain which adversely affect the timely manufacture and supply of our products, our business, prospects, operating results, and financial condition may be materially harmed.

***Expanding our manufacturing capacity will be costly and we may be unsuccessful in doing so in a timely manner, which could delay or prevent the launch and successful commercialization of our late-stage product candidates or other indications for our marketed products if they are approved for marketing and could jeopardize our current and future clinical development programs.***

Expanding our manufacturing capacity to supply commercial quantities of the active pharmaceutical ingredients for our late-stage product candidates if they are approved for marketing, and to supply clinical drug material to support the continued growth of our clinical programs, will require substantial additional expenditures, and we will need to hire and train significant numbers of employees and managerial personnel to staff our manufacturing and supply chain operations. Start-up costs can be large and scale-up entails significant risks related to process development and manufacturing yields. In addition, we may face difficulties or delays in developing or acquiring the necessary production equipment and technology to manufacture sufficient quantities of our product candidates at reasonable costs and in compliance with applicable regulatory requirements. The FDA and analogous foreign regulatory authorities must determine that our existing and any expanded manufacturing facilities comply, or continue to comply, with cGMP requirements for both clinical and commercial production and license them, or continue to license them, accordingly, and such facilities must also comply with applicable environmental, safety, and other governmental permitting requirements. We may not successfully expand or establish sufficient manufacturing capabilities or manufacture our products economically or in compliance with cGMPs and other regulatory requirements, and we and our collaborators may not be able to build or procure additional capacity in the required timeframe to meet commercial demand for our late-stage product candidates if they receive regulatory approval, and to continue to meet the requirements of our clinical programs. This would interfere with our efforts to successfully commercialize EYLEA<sup>®</sup>, ZALTRAP<sup>®</sup>, and ARCALYST<sup>®</sup> for the prevention of gout flares in patients initiating uric acid-lowering treatment if they receive regulatory approval, and could also delay or require us to discontinue one or more of our clinical development programs. As a result, our business, prospects, operating results, and financial condition could be materially harmed.

***Our ability to manufacture our products may be impaired if any of our manufacturing activities, or the activities of third parties involved in our manufacture and supply chain, are found to infringe third-party patents.***

Our ability to continue to manufacture ARCALYST<sup>®</sup>, EYLEA<sup>®</sup>, and ZALTRAP<sup>®</sup> in our Rensselaer, New York facilities, or to utilize third parties to produce our products or perform fill/finish services or other steps in our manufacture and supply chain, depends on our and their ability to operate without infringing the patents or other intellectual property rights of third parties. Other parties may allege that our manufacturing activities, or the activities of third parties involved in our manufacture and supply chain, infringe patents or other intellectual property rights. A judicial decision in favor of one or more parties making such allegations could preclude the manufacture of our products where those intellectual property rights apply which could materially harm our business, results of operations, and prospects.

***If sales of EYLEA<sup>®</sup> for the treatment of wet AMD do not meet the levels currently expected, or if the launch of our late-stage product candidates or new indications of our marketed products, or any of our clinical programs, are delayed or discontinued, we may face costs related to unused capacity at our manufacturing facilities and at the facilities of third parties.***

We have large-scale manufacturing operations in Rensselaer, New York. We use our facilities to produce bulk product of ARCALYST® for the treatment of CAPS, bulk product of EYLEA® for the treatment of wet AMD and clinical and preclinical candidates for ourselves and our collaborations, and plan to use such facilities to produce bulk product for commercial supply of our late-stage product candidates or new indications of our marketed products if they are approved for marketing. If our clinical candidates are discontinued or their clinical development is delayed, if the launch of any of our late-stage product candidates or new indications or our marketed products is delayed or does not occur, or if such products are launched and subsequently recalled or marketing approval is rescinded, we may have to absorb one hundred percent of related overhead costs and inefficiencies, as well as similar costs of third-party contract manufacturers performing services for us.

***Third-party service or supply failures, or other failures, business interruptions, or natural disasters affecting our manufacturing facilities in Rensselaer, New York or the facilities of any other party participating in the supply chain, would adversely affect our ability to supply our products.***

We manufacture all of our bulk drug materials at our manufacturing facilities in Rensselaer, New York. We would be unable to manufacture these materials if our Rensselaer facilities were to cease production due to regulatory requirements or action, business interruptions, labor shortages or disputes, contaminations, fire, natural disasters, or other problems at the facilities.

Also, certain raw materials necessary for the manufacture and formulation of ARCALYST® and EYLEA® and of our product candidates, including ZALTRAP®, are provided by single-source unaffiliated third-party suppliers. In addition, we rely on certain third parties to perform filling, finishing, distribution, laboratory testing, and other services related to the manufacture of ARCALYST® and our product candidates. We would be unable to obtain these raw materials or services for an indeterminate period of time if any of these third parties were to cease or interrupt production or otherwise fail to supply these materials, products, or services to us for any reason, including due to regulatory requirements or action, adverse financial developments at or affecting the supplier, failure by the supplier to comply with cGMPs, business interruptions, or labor shortages or disputes. This, in turn, could materially and adversely affect our ability to manufacture or supply ARCALYST® for the treatment of CAPS and EYLEA® for the treatment of wet AMD and to manufacture and supply commercial quantities of EYLEA® for other ophthalmologic diseases, ZALTRAP®, and ARCALYST® for the prevention of gout flares if they receive regulatory approval, which could materially and adversely affect our business and future prospects.

Certain of the raw materials required in the manufacture and the formulation of our product 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.

***If we fail to meet the stringent requirements of governmental regulation in the manufacture of drug products or product candidates, we could incur substantial remedial costs, delays in the development or approval of our product candidates or new indications for our marketed products and/or in their commercial launch if they obtain regulatory approval, and a reduction in sales.***

We and our third-party providers are required to maintain compliance with cGMP, and are subject to inspections by the FDA or comparable agencies in other jurisdictions to confirm such compliance. Changes of suppliers or modifications of methods of manufacturing may require amending our application(s) to the FDA or such comparable foreign agencies and acceptance of the change by the FDA or such comparable foreign agencies prior to release of product(s). Because we produce multiple product candidates at our facility in Rensselaer, New York, including ARCALYST®, EYLEA®, and ZALTRAP®, there are increased risks associated with cGMP compliance. Our inability, or the inability of our third-party fill/finish or other service providers, to demonstrate ongoing cGMP compliance could require us to engage in lengthy and expensive remediation efforts, withdraw or recall product, halt or interrupt clinical trials, and/or interrupt commercial supply of any marketed products, and could also delay or prevent our obtaining regulatory approval for our late-stage product candidates or new indications for our marketed products. Any delay, interruption, or other issue that arises in the manufacture, fill/finish, packaging, or storage of any drug product or product candidate as a result of a failure of our facilities or the facilities or operations of third parties to pass any regulatory agency inspection or maintain cGMP compliance could significantly impair our ability to develop, obtain approval for, and successfully commercialize our products, which would substantially harm our business and prospects. Any finding of non-compliance could also increase our costs, cause us to delay the development of our product candidates, result in delay in our obtaining, or our not obtaining, regulatory approval of product candidates or new indications for our marketed products, and cause us to lose revenue from any marketed products, which could be seriously detrimental to our business, prospects, and financial condition.

## Risks Related to Commercialization of Products

*We may be unsuccessful in continuing our commercialization of EYLEA® for the treatment of wet AMD or commercializing our late stage product candidates or new indications for our marketed products, if approved, which would materially delay or prevent our achieving profitability.*

Even if clinical trials demonstrate the 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 or new indications for our marketed products will depend upon, among other things, their acceptance by patients, the medical community, and third-party payers and on our and our collaborators' ability to successfully manufacture and commercialize those products or new indications. Even if we obtain regulatory approval for our product candidates or new indications, if they are not successfully commercialized, we will not be able to recover the significant investment we have made in developing such products and our business, prospects, operating results, and financial condition would be severely harmed.

In particular, we are in the early stages of commercialization and cannot be sure that EYLEA® for the treatment of wet AMD will be commercially successful in the pharmaceutical market. In addition to the challenges we face related to a company launching its first major commercial drug, as described in detail in the risk factor immediately below, we and Bayer HealthCare will face intense competition from Lucentis® and from off-label use of Avastin®, both of which have been on the market for a number of years. We expect that the initial commercial success of EYLEA® for the treatment of wet AMD will depend on many factors, including the following:

- the effectiveness of our and Bayer HealthCare's commercial strategies for the launch and marketing of EYLEA® in and outside the United States, respectively, including pricing strategy and the effectiveness of efforts to obtain, and the timing of obtaining, adequate third-party reimbursements;
- maintaining and successfully monitoring commercial manufacturing arrangements for EYLEA® with third parties who perform fill/finish or other steps in the manufacture of EYLEA® to ensure that they meet our standards and those of regulatory authorities, including the FDA, which extensively regulate and monitor pharmaceutical manufacturing facilities;
- our ability to meet the demand for commercial supplies of EYLEA®;
- our ability to effectively communicate to the marketplace the benefits of the dosing regimen of EYLEA® of every 2 months after three initial monthly doses as compared to the monthly dosing regimen of Lucentis®, and the willingness of retinal specialists and patients to switch from Lucentis® or off-label use of Avastin® to EYLEA® for the treatment of wet AMD;
- the ability of patients, retinal specialists, and other providers to obtain and maintain sufficient coverage and reimbursement from third-party payors, including Medicare and Medicaid in the United States and other government and private payors in the United States and foreign jurisdictions; and
- the effect of new health care legislation currently being implemented in the United States.

While we believe that EYLEA® for the treatment of wet AMD has a commercially competitive profile, we cannot predict whether ophthalmologists, particularly retinal specialists, and patients, will accept or utilize EYLEA®. Our and Bayer HealthCare's efforts to educate the relevant medical community and third-party payors regarding the benefits of EYLEA® for the treatment of wet AMD will require significant resources and may not be successful in achieving our objectives. If EYLEA® is approved for marketing but does not achieve significant market acceptance for the treatment of wet AMD, our ability to achieve profitability would be materially impaired or delayed.

*If we are unable to establish, and effectively deploy and manage, sales, marketing, and distribution capabilities in the applicable markets or to enter into agreements with third parties to do so, we will not generate our expected sales of EYLEA® for treatment of wet AMD or successfully launch and commercialize our late-stage product candidates or new indications for our marketed products if they receive regulatory approval, which would materially harm our business, prospects, operating results, and financial condition.*

We currently sell EYLEA® in the United States to three distributors and several specialty pharmacies. We currently sell ARCALYST® for the treatment of CAPS in the United States to two specialty pharmacies. Under these distribution models, we enter into written contracts with our distributors and specialty pharmacies (collectively, our customers), and our customers generally take physical delivery of product. For EYLEA®, the distributors and specialty pharmacies generally sell the product directly to healthcare providers, whereas for ARCALYST®, the specialty pharmacies sell the product directly to patients.

We have established our own sales and marketing organization for EYLEA<sup>®</sup> in the United States for the treatment of wet AMD, and in anticipation of filing for and receiving regulatory approval to market and sell EYLEA<sup>®</sup> in the United States for the treatment of CRVO. However, we may be unsuccessful in achieving a successful commercialization of EYLEA<sup>®</sup> in the United States, which would materially harm our business, prospects, operating results, and financial condition.

We will have to rely on a third party or devote significant resources to develop our own sales and marketing capabilities, and our distribution network, for ARCALYST<sup>®</sup> for patients with gout initiating uric acid-lowering drug therapy if it receives regulatory approval. If we are unable to obtain these capabilities, either by developing our own organizations or entering into agreements with others to provide these functions, even if ARCALYST<sup>®</sup> for the prevention of gout flares receives marketing approval, we will not be able to successfully launch and commercialize this product, which would also materially harm our business, prospects, operating results, and financial condition.

We have limited experience in sales, marketing, or distribution of products in substantial commercial quantities or in establishing and managing the required infrastructure to do so, including large-scale information technology systems and a large-scale distribution network, and we may be unable to establish such infrastructure on a timely basis. To the extent we determine to utilize third parties to provide sales, marketing, or distribution capabilities for ARCALYST<sup>®</sup> for the prevention of gout flares or any of our other product candidates or new indications for marketed products if they receive regulatory approval, we may encounter difficulties in retaining such parties on acceptable terms. Even if we hire qualified sales and marketing personnel, and establish the required infrastructure we need to support our objectives, or enter into marketing and distribution agreements with third parties on acceptable terms, we may not do so in an efficient manner or on a timely basis. We may not be able to correctly judge the size and experience of the sales and marketing force and the scale of distribution capabilities necessary to successfully market and sell in the United States EYLEA<sup>®</sup>, ARCALYST<sup>®</sup> for the prevention of gout flares, or any of our other product candidates or new indications if they receive regulatory approval in the United States and as to which we retain sales and marketing responsibility in that market. Establishing and maintaining sales, marketing, and distribution capabilities are expensive and time-consuming. Our expenses associated with building up and maintaining a sales force and distribution capabilities may be disproportional, particularly in the near term, compared to the revenues we may be able to generate on sales in the United States of EYLEA<sup>®</sup> or ARCALYST<sup>®</sup> for the prevention of gout flares. Ultimately neither we nor our collaborators may be successful in commercializing EYLEA<sup>®</sup>, ZALTRAP<sup>®</sup>, ARCALYST<sup>®</sup> for the prevention of gout flares, or any of our other product candidates.

Under the terms of our collaboration agreement, Sanofi has primary responsibility for sales, marketing, and distribution of ZALTRAP<sup>®</sup> in cancer indications, should it be approved in the future by regulatory authorities for marketing.

We currently have no sales, marketing, commercial, or distribution capabilities outside the United States. Under the terms of our license and collaboration agreement with Bayer HealthCare, we will rely on Bayer HealthCare for sales, marketing, and distribution of EYLEA<sup>®</sup> in countries outside the United States should it be approved for marketing in such countries.

***The commercial success of EYLEA<sup>®</sup> currently being marketed for the treatment of wet AMD, and for our other product candidates or new indications for our marketed products, if any are approved for marketing, is highly uncertain given their method of administration, and because our competitors have received approval for and may be marketing products with a similar mechanism of action or may enter the marketplace with better or lower cost drugs.***

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 and this could adversely affect the commercial success of those products if they receive marketing approval.

There is substantial competition in the biotechnology and pharmaceutical industries from biotechnology, pharmaceutical, 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 commercialization of our product candidates, our competitors have achieved, and may continue to achieve, product commercialization before our products are approved for marketing and sale.

As previously noted, Genentech has an approved VEGF antagonist, Avastin<sup>®</sup>, on the market for treating certain cancers and many different pharmaceutical and biotechnology companies are working to develop competing VEGF antagonists, including Novartis, Amgen, Imclone LLC/Eli Lilly, Pfizer, AstraZeneca, and GlaxoSmithKline. Some of these molecules are further along in development than ZALTRAP<sup>®</sup> and may offer competitive advantages over our molecule. Each of Pfizer, Onyx (together with its partner Bayer HealthCare), and GlaxoSmithKline are

marketing and selling oral medications that target tumor cell growth and new vasculature formation that fuels the growth of tumors. The marketing approvals for Genentech's VEGF antagonist, Avastin<sup>®</sup>, and their extensive, ongoing clinical development plan for Avastin<sup>®</sup> in other cancer indications, make it more difficult for us to enroll patients in clinical trials to support ZALTRAP<sup>®</sup> for those indications and to obtain regulatory approval of ZALTRAP<sup>®</sup> in those indications. This may delay or impair our ability to successfully develop and commercialize ZALTRAP<sup>®</sup> for various cancer indications. In addition, even if ZALTRAP<sup>®</sup> is approved for sale for the treatment of certain cancers, it will be difficult for our drug to compete against Avastin<sup>®</sup> 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<sup>®</sup> for the treatment of wet AMD, CRVO, DME, and other eye indications. Lucentis<sup>®</sup> was approved by the FDA in June 2006 for the treatment of wet AMD and in June 2010 for the treatment of macular edema following retinal vein occlusion (RVO), CRVO, and branch retinal vein occlusion (BRVO). Lucentis<sup>®</sup> was also approved by the EMA for wet AMD in January 2007 and for DME in January 2011. Many other companies are working on the development of product candidates for the potential treatment of wet AMD and DME including those that act by blocking VEGF and VEGF receptors, as well as small interfering ribonucleic acids (siRNAs) that modulate gene expression. In addition, ophthalmologists are using off-label, with success for the treatment of wet AMD, DME, and RVO, third-party repackaged versions of Genentech's approved VEGF antagonist, Avastin<sup>®</sup>.

The National Eye Institute (NEI) and others are conducting long-term, controlled clinical trials comparing Lucentis<sup>®</sup> to Avastin<sup>®</sup> in the treatment of wet AMD. One-year data from the Comparison of Age-Related Macular Degeneration Treatments Trial (CATT) were reported in April 2011 and indicated that Avastin<sup>®</sup> dosed monthly was non-inferior to Lucentis<sup>®</sup> dosed monthly in the primary efficacy endpoint of mean visual acuity gain at 52 weeks. It may be difficult for EYLEA<sup>®</sup> in this or other eye indications for which it may be approved to compete against Lucentis<sup>®</sup> and off-label use of Avastin<sup>®</sup> because doctors and patients have had significant experience using these medicines. Moreover, the recently reported results of the CATT study, combined with the relatively low cost of Avastin<sup>®</sup> in treating patients with wet AMD, may well exacerbate the competitive challenge which EYLEA<sup>®</sup> will face in this or other eye indications for which it may be approved. In addition, while we believe that ZALTRAP<sup>®</sup> would not be well tolerated if administered directly to the eye, if ZALTRAP<sup>®</sup> is approved for the treatment of certain cancers, there is a risk that third parties will attempt to repackage ZALTRAP<sup>®</sup> for off-label use and sale for the treatment of wet AMD and other diseases of the eye, which would present a potential low-cost competitive threat to EYLEA<sup>®</sup> for wet AMD or other eye indications.

The availability of highly effective FDA approved Tumor Necrosis Factors-antagonists (TNF-antagonists) such as Enbrel<sup>®</sup>, Remicade<sup>®</sup>, Humira<sup>®</sup> (adalimumab), a registered trademark of Abbott Laboratories, Simponi<sup>®</sup> (golimumab), a registered trademark of Johnson & Johnson, the IL-1 receptor antagonist Kineret<sup>®</sup>, Ilaris<sup>®</sup> (canakinumab), and other marketed therapies makes it more difficult to successfully develop and commercialize ARCALYST<sup>®</sup> in indications other than CAPS, and this is one of the reasons we discontinued the development of ARCALYST<sup>®</sup> in adult rheumatoid arthritis. In addition, even if ARCALYST<sup>®</sup> is ever approved for sale in indications where TNF-antagonists are approved, it will be difficult for our drug to compete against these FDA approved TNF-antagonists because doctors and patients have had significant experience using these effective medicines. Moreover, in such indications these approved therapeutics may offer competitive advantages over ARCALYST<sup>®</sup>, such as requiring fewer injections.

There are both small molecules and antibodies in development by other companies that are designed to block the synthesis of IL-1 or inhibit the signaling of IL-1. For example, Eli Lilly, Xoma (in collaboration with Servier), and Novartis are each developing antibodies to IL-1 and both Amgen and MedImmune are developing antibodies to the IL-1 receptor. In 2009, Novartis received regulatory approval in the United States and Europe for Ilaris<sup>®</sup>, a fully human anti-interleukin-IL1 $\beta$  antibody, for the treatment of CAPS. Ilaris<sup>®</sup> is also in development for atherosclerosis and a number of other inflammatory diseases. Novartis' IL-1 antibody and these other drug candidates could offer competitive advantages over ARCALYST<sup>®</sup>. For example, Ilaris<sup>®</sup> is dosed once every eight weeks compared to the once-weekly dosing regimen for ARCALYST<sup>®</sup>. The successful development and/or commercialization of these competing molecules could adversely affect sales of ARCALYST<sup>®</sup> for the treatment of CAPS and delay or impair our ability to commercialize ARCALYST<sup>®</sup> for indications other than CAPS.

We are developing ARCALYST<sup>®</sup> for the prevention of gout flares in patients initiating uric acid-lowering therapy and have submitted a supplemental BLA filing for U.S. regulatory approval in this indication. In January 2011, Novartis announced that the results of two Phase 3 studies with Ilaris<sup>®</sup> focused on reducing pain and preventing recurrent attacks or flares in patients with hard-to-treat gout were positive. Novartis has also reported that regulatory filings for the use of Ilaris<sup>®</sup> in gouty arthritis have been completed in the European Union in 2010 and in the United States in the first quarter of 2011, based on the results of these two Phase 3 studies. Ilaris<sup>®</sup> is dosed less frequently for the treatment of CAPS, and if it is approved for the treatment of gout, it may be perceived by some physicians as offering competitive advantages over ARCALYST<sup>®</sup>, which would make it difficult for us to successfully commercialize ARCALYST<sup>®</sup> in that disease.

Currently, inexpensive, oral therapies such as analgesics and other NSAIDs, are used as the standard of care to treat the symptoms of gout diseases. These established, inexpensive, orally delivered drugs may make it difficult for us to successfully commercialize ARCALYST® in these diseases.

Our earlier-stage clinical candidates in development are all fully human monoclonal antibodies, which were generated using our *VelocImmune*® technology. Our antibody generation technologies and earlier-stage clinical candidates face competition from many pharmaceutical and biotechnology companies using various technologies.

Numerous other companies are developing therapeutic antibody products. Companies such as Pfizer, Johnson & Johnson, AstraZeneca, Amgen, Biogen Idec, Novartis, Genentech/Roche, Bristol-Myers Squibb, Abbott, and GlaxoSmithKline have generated therapeutic products that are currently in development or on the market that are derived from recombinant DNA that comprise human antibody sequences.

We are aware of several pharmaceutical and biotechnology companies actively engaged in the research and development of antibody products against targets that are also the targets of our early-stage product candidates. For example, Pfizer, Johnson & Johnson, and Abbott are developing antibody product candidates against NGF. Genentech/Roche is marketing an antibody against IL-6R (tocilizumab) for the treatment of rheumatoid arthritis, and several other companies, including Centocor/Johnson & Johnson, and Bristol-Myers Squibb, have antibodies against IL-6 in clinical development for this disease. GlaxoSmithKline, in partnership with OncoMed Pharmaceuticals, has a Dll4 antibody in clinical development for the treatment of solid tumors. Aerovance has two formulations of a biologic directed against IL-4 in clinical development. Amgen previously had an antibody against IL-4R in clinical development for the treatment of asthma. We believe that several companies, including Amgen and Pfizer, have development programs for antibodies against PCSK9. Amgen, Pfizer, and AstraZeneca have development programs underway for antibodies against ANG2. If any of these or other competitors 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, such developments may have an adverse effect on our business or future prospects.

***The successful commercialization of EYLEA® for the treatment of wet AMD as well as our late-stage product candidates or new indications for our marketed products, if approved, will depend on obtaining coverage and reimbursement for use of these products from third-party payers, including Medicare and Medicaid in the United States, and these payers may not agree to cover or adequately reimburse for use of our products or may do so at levels that make our products uncompetitive and/or unprofitable, which would materially harm our business, prospects, operating results, and financial condition.***

Our product candidates, if commercialized, may be significantly more expensive than traditional drug treatments. For example, we are developing ARCALYST® for the prevention of gout flares in patients initiating uric acid-lowering drug therapy. Patients suffering from this gout indication are currently treated with inexpensive therapies, including NSAIDs. These existing treatment options are likely to be considerably less expensive and may be preferable to a biologic medication for some patients. Our future revenues and profitability will be adversely affected in a material manner 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 do not 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 payers more expensive for patients, and require prior authorization or failure on another type of treatment before covering a particular drug. In particular, payers may impose these obstacles to coverage on higher-priced drugs, as our product candidates are likely to be.

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. In March 2010, the PPACA and a related reconciliation bill were enacted in the United States. This legislation imposes cost containment measures that are likely to adversely affect the amount of reimbursement for our future products. The full effects of this legislation are unknown at this time and will not be known until regulations and guidance are issued by CMS and other federal and state agencies. Further, in September 2011 the Office of Inspector General (OIG) of the Department of Health and Human Services issued a report entitled *Review of Medicare Part B Avastin and Lucentis Treatments for Age-Related Macular Degeneration* in which the OIG details possible savings to the Medicare program by using off-label Avastin® rather than Lucentis® for the treatment of wet AMD. Some states are also considering legislation that would control the prices of drugs, and state Medicaid programs are increasingly requesting manufacturers to pay supplemental rebates and requiring prior authorization by the state program for use of any drug for which supplemental rebates are not being paid. It is likely that federal and state legislatures and health agencies will continue to focus on additional health care reform in the future that will impose additional constraints on prices and reimbursements for our products.



Since EYLEA<sup>®</sup> for the treatment of wet AMD and other eye diseases, ZALTRAP<sup>®</sup> for oncology indications, and ARCALYST<sup>®</sup> for the prevention of gout flares will likely be too expensive for most patients to afford without health insurance coverage, if these products are unable to obtain adequate coverage and reimbursement by third-party payers, including Medicare and Medicaid in the United States, our ability to successfully commercialize these products would be materially adversely impacted. The status of a J-code for our marketed products could also affect reimbursement. J-codes are permanent reimbursement codes maintained by CMS that are a component of HCPCS, and are typically used to report injectable drugs that ordinarily cannot be self-administered. Although we have a J-Code for ARCALYST<sup>®</sup>, we do not currently have a J-Code for EYLEA<sup>®</sup>, although we anticipate assignment of a J-Code for EYLEA<sup>®</sup> in January 2013. Without a unique J-code identifier, EYLEA<sup>®</sup> must be billed using a non-specific miscellaneous J-code. Since such codes may be used for a wide variety of products, health plans may have more difficulty determining the actual product used and billed for the patient. As a result, these claims must often be submitted with additional information and manually processed, which can create delays in claims processing times as well as increasing the likelihood for claim errors. Third-party payers, including Medicare and Medicaid in the United States, may not cover and/or reimburse for these products at levels required for us to successfully commercialize these products. Any limitation imposed by third-party payers on the use of our products if they are approved for marketing, any action or decision by CMS or analogous foreign agencies or authorities which for any reason denies coverage or reimbursement for our products or provides coverage or reimbursement at levels that harm our products' competitiveness or leads to lower prices for those products, will have a material negative 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 and our collaborators may be unable to obtain coverage, pricing, and/or reimbursement on terms that are favorable to us or necessary for us or our collaborators to successfully commercialize our products in those countries. 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 or our collaborators are unable to market our products in foreign countries or if coverage and reimbursement for our products in foreign countries is limited or delayed.

#### **Regulatory and Litigation Risks**

*If the testing or use of our products harms people, we could be subject to costly and damaging product liability claims.*

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 enroll in our clinical trials may not protect us from liability or the cost of litigation. We may also be subject to claims by patients who use our approved products, ARCALYST<sup>®</sup> for the treatment of CAPS, or EYLEA<sup>®</sup> for the treatment of wet AMD, or EYLEA<sup>®</sup> for other indications, ZALTRAP<sup>®</sup>, or ARCALYST<sup>®</sup> for the prevention of gout flares if those product candidates receive regulatory approval and become commercially available, that they have been injured by a side effect associated with the drug. We may face product liability claims and be found responsible even if injury arises from the acts or omissions of our third-party fill/finish or other providers. Our product liability insurance may not cover all potential liabilities or may not completely cover any liability arising from any such litigation. Moreover, in the future we may not have access to liability insurance or be able to maintain our insurance on acceptable terms.

*If we market and sell approved products, in a way that violates federal or state healthcare laws, we may be subject to civil or criminal penalties.*

In addition to FDA and related regulatory requirements, we are subject to health care fraud and abuse laws, such as the federal False Claims Act, the anti-kickback provisions of the federal Social Security Act, and other state and federal laws and regulations. Federal and state anti-kickback laws prohibit, among other things, payments or other remuneration to induce or reward someone to purchase, prescribe, endorse, or recommend a product that is reimbursed under federal or state healthcare programs. If we provide payments or other remuneration to a healthcare professional to induce the prescribing of our products, we could face liability under state and federal anti-kickback laws.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to get a false claim paid. Pharmaceutical companies have been prosecuted under these laws for a variety of alleged promotional and marketing activities, such as allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product; reporting to pricing services inflated average wholesale prices that were then used by federal programs to set reimbursement rates; engaging in promotion for uses that the FDA has not approved, known as off-label uses, that caused claims to be submitted to Medicaid for non-covered off-label uses, and submitting inflated best price information to the Medicaid Rebate program.

The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payer. Sanctions under these federal and state laws may include civil monetary penalties, exclusion of a manufacturer's products from reimbursement under government programs, criminal fines, and imprisonment.

Even if it is determined that we have not violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which would harm our business and financial results and condition. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be challenged under one or more of such laws.

In recent years, several states and localities, including California, the District of Columbia, Massachusetts, Minnesota, Nevada, New Mexico, Vermont, and West Virginia, have enacted legislation requiring pharmaceutical companies to establish marketing compliance programs, and file periodic reports with the state or make periodic public disclosures on sales, marketing, pricing, clinical trials, and other activities. Similar requirements are being considered in other states. In addition, as part of the PPACA, pharmaceutical companies will be required to file reports with the federal government regarding payments made to healthcare professionals. Many of these requirements are new and uncertain, and the penalties for failure to comply with these requirements are unclear. Nonetheless, if we are found not to be in full compliance with these laws, we could face enforcement actions, fines, and other penalties, and could receive adverse publicity, which would harm our business and financial results and condition.

***Risks from the improper conduct of employees, agents or contractors or collaborators could adversely affect our business or reputation.***

We cannot ensure that our compliance controls, policies, and procedures will in every instance protect us from acts committed by our employees, agents, contractors, or collaborators that would violate the laws or regulations of the jurisdictions in which we operate, including without limitation, healthcare, employment, foreign corrupt practices, environmental, competition, and privacy laws. Such improper actions could subject us to civil or criminal investigations, monetary and injunctive penalties and could adversely impact our ability to conduct business, results of operations, and reputation.

***Our operations may involve hazardous materials and are subject to environmental, health, and safety laws and regulations. Compliance with these laws and regulations is costly, and 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.

***Our business is subject to increasingly complex corporate governance, public disclosure, and accounting requirements and regulations that could adversely affect our business and financial results and condition.***

We are subject to changing rules and regulations of various federal and state governmental authorities as well as the stock exchange on which our Common Stock is listed. These entities, including the Public Company Accounting Oversight Board (PCAOB), the Securities and Exchange Commission (SEC), and The NASDAQ Stock Market LLC, have issued a significant number of new and increasingly complex requirements and regulations over the course of the last several years and continue to develop additional requirements and regulations in response to laws enacted by Congress, including the Sarbanes-Oxley Act of 2002 and, most recently, the Dodd-Frank Wall Street Reform and Protection Act, or the Dodd-Frank Act. There are significant corporate governance and executive compensation-related provisions in the Dodd-Frank Act that expressly authorized or required the SEC to adopt additional rules in these areas, such as shareholder approval of executive compensation (so-called "say on pay") and proxy access. On January 25, 2011, the SEC adopted final rules concerning "say on pay". Our efforts to comply with these requirements and regulations have resulted in, and are likely to continue to result in, an increase in expenses and a diversion of management's time from other business activities.

***Changes in laws and regulations affecting the healthcare industry could adversely affect our business.***

All aspects of our business, including research and development, manufacturing, marketing, pricing, sales, litigation, and intellectual property rights, are subject to extensive legislation and regulation. Changes in applicable federal and state laws and agency regulations could have a materially negative impact on our business. These include:

- changes in the FDA and foreign regulatory processes for new therapeutics that may delay or prevent the approval of any of our current or future product candidates;
- new laws, regulations, or judicial decisions related to healthcare availability or the payment for healthcare products and services, including prescription drugs, that would make it more difficult for us to market and sell products once they are approved by the FDA or foreign regulatory agencies;
- changes in FDA and foreign regulations that may require additional safety monitoring prior to or after the introduction of new products to market, which could materially increase our costs of doing business; and
- changes in FDA and foreign cGMPs that may make it more difficult and costly for us to maintain regulatory compliance and/or manufacture our marketed product and product candidates in accordance with cGMPs.

As described above, the PPACA and potential regulations thereunder easing the entry of competing follow-on biologics into the marketplace, other new legislation or implementation of existing statutory provisions on importation of lower-cost competing drugs from other jurisdictions, and legislation on comparative effectiveness research are examples of previously enacted and possible future changes in laws that could adversely affect our business.

**Risks Related to Our Reliance on Third Parties**

***If our antibody collaboration with Sanofi is terminated, our business operations and financial condition, and our ability to discover, develop, manufacture, and commercialize our pipeline of product candidates in the time expected, or at all, would be materially harmed.***

We rely heavily on funding from Sanofi to support our target discovery and antibody research and development programs. Sanofi has committed to pay up to \$160 million per year, or a total of \$1.28 billion, between 2010 and 2017 to fund our efforts to identify and validate drug discovery targets and pre-clinically develop fully human monoclonal antibodies against such targets. Sanofi has a one-time option to adjust the maximum reimbursement amount down to \$120 million per year commencing in 2014 if over the prior two years certain specified criteria are not satisfied. If this downward adjustment occurs, it will reduce our resources available for antibody discovery activities and negatively affect our clinical pipeline. Sanofi also initially funds almost all of the development expenses incurred by both companies in connection with the clinical development of antibodies that Sanofi elects to co-develop with us. We rely on Sanofi to fund these activities. In addition, with respect to those antibodies that Sanofi elects to co-develop with us, such as sarilumab, REGN727, REGN668, REGN421, REGN910, REGN728, and REGN1033, we rely on Sanofi to lead much of the clinical development efforts and assist with obtaining regulatory approval, particularly outside the United States. We also rely on Sanofi to lead the commercialization efforts to support all of the antibody products that are co-developed by Sanofi and us if they receive regulatory approval. If Sanofi does not elect to co-develop the antibodies that we discover or opts-out of their development, we would be required to fund and oversee on our own the clinical trials, any regulatory responsibilities, and the ensuing commercialization efforts to support those antibody products. For example, during 2011 and 2012 to date, Sanofi elected not to continue co-development of REGN846 and REGN475, and decided not to opt-in to the REGN1154 program. If Sanofi terminates the antibody collaboration or fails to comply with its payment obligations thereunder, our business, prospects, operating results, and financial condition would be materially harmed. We would be required to either expend substantially more resources than we have anticipated to support our research and development efforts, which could require us to seek additional funding that might not be available on favorable terms or at all, or materially cut back on such activities. Even though none of the antibodies from this collaboration may ever be successfully developed and commercialized, if Sanofi does not perform its obligations with respect to antibodies that it elects to co-develop, our ability to develop, manufacture, and commercialize these antibody product candidates will be significantly adversely affected.

*If our collaboration with Sanofi for ZALTRAP® is terminated, or Sanofi materially breaches its obligations thereunder, our business operations, prospects, and financial condition, and our ability to develop, manufacture, and commercialize ZALTRAP® in the time expected, or at all, would be materially harmed.*

We rely heavily on Sanofi to lead much of the development of ZALTRAP®. Sanofi initially funds all of the development expenses incurred by both companies in connection with the ZALTRAP® program. If the ZALTRAP® program continues, we will rely on Sanofi to assist with funding the ZALTRAP® program, provide commercial manufacturing capacity, enroll and monitor clinical trials, obtain regulatory approval, particularly outside the United States, and lead the commercialization of ZALTRAP®. While ZALTRAP® may not ever be successfully developed and commercialized, if Sanofi fails to perform its obligations in a timely manner, or at all, our ability to develop, manufacture, and commercialize ZALTRAP® in cancer indications will be significantly adversely affected. Sanofi has the right to terminate its collaboration agreement with us at any time upon twelve months advance notice. If Sanofi were to terminate its collaboration agreement with us, we would not have the resources or skills to replace those of our partner, which could require us to seek additional funding that might not be available on favorable terms or at all, and could cause significant delays in the development and/or manufacture of ZALTRAP® and result in substantial additional costs to us. We have limited commercial capabilities and would have to develop or outsource these capabilities. Termination of the Sanofi collaboration agreement for ZALTRAP® would create substantial new and additional risks to the successful development and commercialization of ZALTRAP®.

***If our collaboration with Bayer HealthCare for EYLEA® is terminated, or Bayer HealthCare materially breaches its obligations thereunder, our business operations, prospects, and financial condition, and our ability to continue to develop EYLEA® and commercialize EYLEA® outside the United States in the time expected, or at all, would be materially harmed.***

We rely heavily on Bayer HealthCare to assist with the development, and the commercialization outside the United States, of EYLEA®. 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 EYLEA® development program. As the EYLEA® program continues, we will continue to rely on Bayer HealthCare to assist with funding the EYLEA® development program, continue to lead the development of EYLEA® outside the United States, obtain regulatory approval outside the United States, and provide all sales, marketing, and commercial support for the product outside the United States. In particular, Bayer HealthCare has responsibility for selling EYLEA® outside the United States using its sales force. While we cannot assure you that EYLEA® will receive regulatory approval in or outside the United States or be successfully commercialized, if Bayer HealthCare does not perform its obligations in a timely manner, or at all, our ability to develop, manufacture, and commercialize EYLEA® 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 require us to seek additional funding or another collaboration that might not be available on favorable terms or at all, and could cause significant delays in the development and/or commercialization of EYLEA® outside the United States and result in substantial additional costs to us. We currently have limited commercial 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 and commercialization of EYLEA®, particularly outside the United States.

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

We depend upon third-party collaborators, including Sanofi, Bayer HealthCare, and service providers such as CROs, outside testing laboratories, clinical investigator sites, and third-party manufacturers, fill/finish, and product packagers and labelers, to assist us in the manufacture and preclinical and clinical development of our product candidates. We also depend, or will depend, on some of these third parties in connection with the commercialization of EYLEA® for the treatment of wet AMD, ARCALYST® for the treatment of CAPS, and our late-stage product candidates and new indications for our marketed products if they are approved for marketing. 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 in compliance with applicable GMPs, Good Laboratory Practices (GLPs), or GCP Standards, we could experience additional costs, delays, and difficulties in the manufacture or development of, or in obtaining approval by regulatory authorities for and successfully commercializing, our product candidates.

We rely on third-party service providers to support the distribution of EYLEA® and ARCALYST® and for many other related activities in connection with the commercialization of these marketed products. Despite our arrangements with them, these third parties may not perform adequately. If these service providers do not perform their services adequately, our sales of EYLEA® for the treatment of wet AMD and ARCALYST® for the treatment of CAPS will suffer.

#### **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, other key members of our senior management team, and our Chairman. If we are not able to retain any of these persons, 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 S. 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. As we commercialize EYLEA® in the United States for the treatment of wet AMD and prepare for commercialization in the United States of EYLEA® for the treatment of CRVO and ARCALYST® for the treatment of gout flares in patients initiating uric acid-lowering therapy, should they receive regulatory approval, we will also be highly dependent on the expertise and services of members of our senior management leading these commercialization efforts. 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 to continue to advance our business and achieve our strategic objectives.



## Information Technology Risks

*Significant disruptions of information technology systems or breaches of data security could adversely affect our business.*

Our business is increasingly dependent on critical, complex, and interdependent information technology systems, including Internet-based systems, to support business processes as well as internal and external communications. The size and complexity of our computer systems make them potentially vulnerable to breakdown, malicious intrusion, and computer viruses which may result in the impairment of production and key business processes.

In addition, our systems are potentially vulnerable to data security breaches whether by employees or others which may expose sensitive data to unauthorized persons. Such data security breaches could lead to the loss of trade secrets or other intellectual property, or could lead to the public exposure of personal information (including sensitive personal information) of our employees, clinical trial patients, customers, and others.

Such disruptions and breaches of security could have a material adverse effect on our business, prospects, operating results, and financial condition.

## 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:

- announcement of actions by the FDA or foreign regulatory authorities or their respective advisory committees regarding our, or our collaborators currently pending or future application(s) for regulatory approval of our product candidate(s) or new indications for our marketed products;
- announcement of submission of an application for regulatory approval of one or more of our product candidates or new indications for our marketed products;
- progress, delays, or adverse results in clinical trials;
- announcement of technological innovations or product candidates by us or competitors;
- fluctuations in our operating results; in particular, net product sales of, and profits from, EYLEA® and, if any of our product candidates or our new indications for our marketed products receive regulatory approval, net product sales of, and profits from, these product candidates and new indications;
- market acceptance of, and fluctuations in market share for, our marketed products, especially EYLEA®, and whether these factors, including our net products sales, underperform, meet, or exceed the expectations of investors or analysts;
- third-party claims that our products or technologies infringe their patents;
- third-party challenges to our patents in the European Patent Office and in the U.S. Patent and Trademark Office;
- public concern as to the safety or effectiveness of any of our marketed products or product candidates or new indications for our marketed products, including EYLEA®, ZALTRAP®, or ARCALYST® for the prevention of gout flares in patients initiating uric acid-lowering therapy;
- pricing or reimbursement actions or decisions by government authorities or insurers affecting the coverage or reimbursement of any of our marketed products or competitors products;
- our ability to raise additional capital as needed on favorable terms;
- developments in our relationship with collaborative partners;
- developments in the biotechnology industry or in government regulation of healthcare;
- large sales of our Common Stock by our executive officers, directors, or significant shareholders;
- arrivals and departures of key personnel; and
- general market conditions.

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

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

A small number of our shareholders beneficially own a substantial amount of our Common Stock. As of December 31, 2011, our six largest shareholders plus Leonard S. Schleifer, M.D., Ph.D., our Chief Executive Officer, beneficially owned 61.9% of our outstanding shares of Common Stock, assuming, in the case of our Chief Executive Officer, the conversion of his Class A Stock into Common Stock and the exercise of all options held by him which are exercisable within 60 days of December 31, 2011. In September 2003, Sanofi (then Aventis Pharmaceuticals Inc.) purchased 2,799,552 newly issued, unregistered shares of our Common Stock, and in December 2007 Sanofi purchased an additional 12,000,000 newly issued, unregistered shares of our Common Stock. Under our investor agreement, as amended, with Sanofi, these shares may not be sold until December 20, 2017 except under limited circumstances and subject to earlier termination of these restrictions upon the occurrence of certain events. In addition, in October 2010, Sanofi purchased an additional 1,017,401 shares of Common Stock in our underwritten public offering. As of December 31, 2011, Sanofi beneficially owned 15,816,953 shares of our Common Stock, representing approximately 17.4% of the shares of Common Stock then outstanding. If Sanofi, 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, 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, 2011, holders of Class A Stock held 18.9% of the combined voting power of all shares 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 the vote on certain corporate transactions that require majority or supermajority approval of the combined classes, including mergers and other business combinations. This may result in our taking corporate actions that other shareholders may not consider to be in their best interest and may affect the price of our Common Stock. As of December 31, 2011:

- our current executive officers and directors beneficially owned 12.0% 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, 2011, and 25.0% 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, 2011; and
- our six largest shareholders plus Leonard S. Schleifer, M.D., Ph.D. our Chief Executive Officer, beneficially owned 61.9% of our outstanding shares of Common Stock, assuming, in the case of our Chief Executive Officer, the conversion of his Class A Stock into Common Stock and the exercise of all options held by him which are exercisable within 60 days of December 31, 2011. In addition, these seven shareholders held 65.1% 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 which are exercisable within 60 days of December 31, 2011.

Pursuant to an investor agreement, as amended, Sanofi has agreed to vote its shares, at Sanofi's election, either as recommended by our board of directors or proportionally with the votes cast by our other shareholders, except with respect to certain change of control transactions, liquidation or dissolution, stock issuances equal to or exceeding 10% of the then outstanding shares or voting rights of Common Stock and Class A Stock, and new equity compensation plans or amendments if not materially consistent with our historical equity compensation practices.

*The anti-takeover effects of provisions of our charter, by-laws, and of New York corporate law and the contractual standstill provisions in our investor agreement with Sanofi, 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 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 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 Stock and Class A Stock;
- 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;
- a provision whereby 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;
- a requirement that 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, in addition to certain restrictions which may apply to business combinations involving our company and an interested shareholder, a plan of merger or consolidation of our 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.*

Until the later of the fifth anniversaries of the expiration or earlier termination of our antibody collaboration agreements with Sanofi or our ZALTRAP® collaboration with Sanofi, Sanofi will be bound by certain standstill provisions, as amended, which contractually prohibit Sanofi from acquiring more than certain specified percentages of our Class A Stock and Common Stock (taken together) or otherwise seeking to obtain control of our company.

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 our company. Many of our stock options issued under our 2000 Long-Term Incentive Plan, as amended and restated, may become fully vested in connection with a change in control of our company, as defined in the plan. These contractual provisions may also have the effect of deterring, delaying, or preventing an acquisition or other change in control.

#### **Risks Relating to Our Convertible Senior Notes and Related Hedge Transactions**

*The convertible note hedges and warrant transactions we entered into in connection with our 1.875% Convertible Senior Notes issuance may affect the trading price of our Common Stock.*

In connection with our offering of our 1.875% Convertible Senior Notes due October 1, 2016, we entered into convertible note hedge transactions with four financial institutions (the hedge counterparties). The convertible note hedge transactions are expected to reduce the potential dilution to our Common Stock and/or offset potential cash payments in excess of the principal amount of the notes, as the case may be upon conversion of the notes. In the event that the hedge counterparties fail to deliver shares to us or potential cash payments as the case may be as required under the convertible note hedge documents, we would not receive the benefit of such transactions. Separately, we also entered into warrant transactions with the hedge counterparties. The warrant transactions could separately have a dilutive effect from the issuance of Common Stock pursuant to the warrants.

In connection with hedging these transactions, the hedge counterparties and/or their affiliates may enter into various derivative transactions with respect to our Common Stock, and may enter into, or may unwind, various derivative transactions and/or purchase or sell our Common Stock or other securities of ours in secondary market transactions prior to maturity of the notes (and are likely to do so during any conversion period related to any conversion of the notes). These activities could have the effect of increasing or preventing a decline in, or could have a negative effect on, the value of our Common Stock and could have the effect of increasing or preventing a decline in the value of our Common Stock during any cash settlement averaging period related to a conversion of the notes.



In addition, we intend to exercise options under the convertible note hedge transactions whenever notes are converted. In order to unwind its hedge position with respect to the options we exercise, the hedge counterparties and/or their affiliates may sell shares of our Common Stock or other securities in secondary market transactions or unwind various derivative transactions with respect to our Common Stock during the cash settlement averaging period for the converted notes. The effect, if any, of any of these transactions and activities on the trading price of our Common Stock or the notes will depend in part on market conditions and cannot be ascertained at this time, but any of these activities could adversely affect the value of our Common Stock and the value of the notes. The derivative transactions that the hedge counterparties and/or their affiliates expect to enter into to hedge these transactions may include cash-settled equity swaps referenced to our Common Stock. In certain circumstances, the hedge counterparties and/or their affiliates may have derivative positions that, when combined with the hedge counterparties and their affiliates' ownership of our Common Stock, if any, would give them economic exposure to the return on a significant number of shares of our Common Stock.

*The fundamental change provisions of our 1.875% Convertible Senior Notes and certain of the terms of the convertible note hedge and warrant transactions may delay or prevent an otherwise beneficial takeover attempt of us.*

The fundamental change purchase rights, which will allow noteholders to require us to purchase all or a portion of their notes upon the occurrence of a fundamental change, as defined in the indenture governing the notes, and the provisions requiring an increase to the conversion rate for conversions in connection with make-whole fundamental changes, as set forth in the indenture, may in certain circumstances delay or prevent a takeover of us and the removal of incumbent management that might otherwise be beneficial to investors. In addition, upon the occurrence of certain extraordinary events, the convertible note hedge transactions would be exercised upon the conversion of notes, and the warrant transactions may be terminated. It is possible that the proceeds we receive upon the exercise of the convertible note hedge transactions would be significantly lower than the amounts we would be required to pay upon termination of the warrant transactions. Such differences may result in the acquisition of us being on terms less favorable to our shareholders than it would otherwise be.

#### ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

#### ITEM 2. PROPERTIES

We conduct our research, development, manufacturing, and administrative activities at our owned and leased facilities. Under our lease in Tarrytown, New York, as amended, we lease approximately 553,000 square feet of laboratory and office facilities. In addition, in September 2011 we entered into a lease amendment under our Tarrytown lease for approximately 40,000 additional square feet of space, which will commence contingent upon certain building improvements being completed by our landlord. We currently expect our landlord to complete these improvements during the first half of 2012. The term of the Tarrytown, New York lease will expire in June 2024. The lease contains three renewal options to extend the term of the lease by five years each and early termination options on approximately 323,000 square feet of space. The lease provides for monthly payments over its term and additional charges for utilities, taxes, and operating expenses.

In July 2011, we leased approximately 19,600 square feet of office space in Liberty Corner, New Jersey. The term of the lease expires in January 2017.

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

Location	Square Footage	Expiration	Current Monthly Base Rental Charges <sup>(1)</sup>	Renewal Option Available
Tarrytown, New York	553,000	June 2024	\$ 1,843,000	Three 5-year terms
Liberty Corner, New Jersey	19,600	January 2017	\$ 37,200	Two 5-year terms

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

We own facilities in Rensselaer, New York, consisting of three buildings totaling approximately 395,000 square feet of research, manufacturing, office, and warehouse space.

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 and manufacturing activities and support 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 ordinary course legal proceedings to have a material adverse effect on our business or financial condition.

#### *Genentech Patent Litigation*

We are aware of issued patents and pending patent applications owned by Genentech that claim certain chimeric VEGF receptors. We do not believe that ZALTRAP® or EYLEA® infringe any valid claim in these patents or patent applications. We are involved in five patent litigations with Genentech, two in the United States and three in Europe. In November 2010, we commenced a lawsuit against Genentech in the U.S. District Court for the Southern District of New York (the Court), seeking a declaratory judgment that no activities relating to our VEGF Trap infringe any valid claim of certain Genentech patents referred to as the Davis-Smyth patents (the First Davis-Smyth Case). Genentech answered the complaint and asserted counterclaims that our prior or planned activities relating to VEGF Trap have infringed or will infringe claims of four of the five Davis-Smyth patents and requested a judgment against us for damages, including for willful infringement, and other relief as the Court deems appropriate.

On December 31, 2011, we entered into a non-exclusive license and partial settlement agreement (the Agreement) with Genentech that covers making, using, and selling EYLEA® in the United States for the prevention and treatment of human eye diseases and disorders in the United States. Under the Agreement, we received a non-exclusive license to the Davis-Smyth patents, and certain other technology patents owned or co-owned by Genentech. The Agreement does not cover any non-U.S. patent rights or non-U.S. patent disputes, and does not cover any use of aflibercept other than for prevention and treatment of human eye diseases and disorders in the United States. The First Davis-Smyth Case is continuing with respect to matters not covered by the Agreement. The Agreement provides for us to make payments to Genentech based on U.S. sales of EYLEA® through May 7, 2016, the date the Davis-Smyth patents expire. We will make a lump-sum payment of \$60 million once cumulative U.S. sales of EYLEA® reach \$400 million. We will also pay royalties of 4.75% on cumulative U.S. sales of EYLEA® between \$400 million and \$3 billion and 5.5% on any cumulative U.S. sales of EYLEA® over \$3 billion. As a result of the Agreement, on January 17, 2012 Genentech filed a second amended answer and counterclaim in the First Davis-Smyth Case, in which it amended its counterclaims alleging infringement of four of the five Davis-Smyth patents. On December 23, 2011, Genentech initiated a related case in the Court against Regeneron and Sanofi alleging infringement of four of the five Davis-Smyth Patents by activities relating to VEGF Trap (but excluding EYLEA®) (the Second Davis-Smyth Case). As in the First Davis-Smyth Case, in the new complaint Genentech requests a judgment against us for damages, including for willful infringement, and other relief as the Court deems appropriate.

We believe Genentech's claims in the First Davis Smyth Case and the Second Davis Smyth Case are without merit and intend to continue to defend against all of Genentech's remaining claims vigorously.

We have initiated patent-related actions against Genentech in Germany, the United Kingdom, and Italy, and may initiate other actions in other countries outside the United States, which could have similar or other adverse outcomes that would materially harm our business and which, irrespective of the outcomes, may also entail significant costs and expenses.

### **ITEM 4. NOT APPLICABLE**

## PART II

## ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS, AND ISSUER PURCHASES OF EQUITY SECURITIES

*Market for Registrant's Common Equity*

Our Common Stock is quoted on The NASDAQ Global Select 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 our Common Stock as reported by The NASDAQ Global Select Market:

	High	Low
<b>2010</b>		
First Quarter	\$ 30.51	\$ 23.42
Second Quarter	30.58	22.32
Third Quarter	27.53	20.45
Fourth Quarter	33.94	24.29
<b>2011</b>		
First Quarter	\$ 45.11	\$ 32.32
Second Quarter	71.74	41.83
Third Quarter	79.90	42.83
Fourth Quarter	66.47	49.58

As of February 10, 2012, there were 392 shareholders of record of our Common Stock and 45 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 2012 Annual Meeting of Shareholders to be filed with the SEC is incorporated herein by reference.

*Issuer Purchases of Equity Securities*

The following table reflects shares of Common Stock withheld by us for employees to satisfy their tax withholding obligations arising upon the vesting of restricted equity awards granted under our Amended and Restated Long-Term Incentive Plan.

Period	Total Number of Shares (or Units) Purchased	Average Price Paid per Share (or Unit)	Total Number of Shares (or Units) Purchased as Part of Publicly Announced Plans or Programs	Maximum Number (or Approximate Dollar Value) of Shares (or Units) that May Yet Be Purchased Under the Plans or Programs
12/1/2011-12/31/2011	51,549	51.18	--	--

*Recent Sales of Unregistered Securities*

There were no unregistered sales of equity securities in 2011 that have not been previously reported in a Quarterly Report on Form 10-Q.





**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, 2006 through December 31, 2011. The comparison assumes that \$100 was invested on December 31, 2006 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.

	12/31/2006	12/31/2007	12/31/2008	12/31/2009	12/31/2010	12/31/2011
<b>Regeneron</b>	\$ 100.00	\$ 120.33	\$ 91.48	\$ 120.48	\$ 163.58	\$ 276.18
<b>NASDAQ Pharm</b>	100.00	105.17	97.85	109.95	119.19	127.71
<b>NASDAQ US</b>	100.00	108.47	135.11	95.38	113.19	113.81

**Item 6. Selected Financial Data**

The selected financial data set forth below for the years ended December 31, 2011, 2010, and 2009 and at December 31, 2011 and 2010 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, 2008 and 2007 and at December 31, 2009, 2008, and 2007 are derived from our audited financial statements not included in this report.

	<b>Year Ended December 31,</b>				
	<b>2011</b>	<b>2010</b>	<b>2009</b>	<b>2008</b>	<b>2007</b>
	<b>(In thousands, except per share data)</b>				
<b>Statement of Operations Data</b>					
<b>Revenues</b>					
Collaboration revenue	\$ 369,681	\$ 386,725	\$ 314,457	\$ 185,138	\$ 87,648
Net product sales	44,686	25,254	18,364	6,249	
Technology licensing	24,858	40,150	40,013	40,000	28,421
Contract research and other	6,599	6,945	6,434	7,070	8,955
	445,824	459,074	379,268	238,457	125,024
<b>Expenses</b>					
Research and development	529,506	489,252	398,762	274,903	202,468
Selling, general, and administrative	117,261	65,201	52,923	48,880	37,929
Cost of goods sold	4,216	2,093	1,686	923	
	650,983	556,546	453,371	324,706	240,397
Loss from operations	(205,159)	(97,472)	(74,103)	(86,249)	(115,373)
<b>Other income (expense)</b>					
Investment income	3,549	2,122	4,488	18,161	20,897
Interest expense	(21,282)	(9,118)	(2,337)	(7,752)	(12,043)
Loss on early extinguishment of debt				(938)	
	(17,733)	(6,996)	2,151	9,471	8,854
Net loss before income tax (benefit) expense	(222,892)	(104,468)	(71,952)	(76,778)	(106,519)
Income tax (benefit) expense	(1,132)		(4,122)	2,351	
Net loss	\$ (221,760)	\$ (104,468)	\$ (67,830)	\$ (79,129)	\$ (106,519)
Net loss per share, basic and diluted	\$ (2.45)	\$ (1.26)	\$ (0.85)	\$ (1.00)	\$ (1.61)

	<b>At December 31,</b>				
	<b>2011</b>	<b>2010</b>	<b>2009</b>	<b>2008</b>	<b>2007</b>
	<b>(In thousands)</b>				
<b>Balance Sheet Data</b>					
Unrestricted and restricted cash, cash equivalents, and marketable securities (current and non-current)	\$ 810,550	\$ 626,939	\$ 390,010	\$ 527,461	\$ 846,279
Total assets	1,323,583	1,089,432	741,202	724,220	957,881
Notes payable (current and non-current)	275,019				200,000
Facility lease obligations (current and non-current)	160,514	160,030	109,022	54,182	21,623
Capital lease obligations (current and non-current)	2,506	2,829			
Stockholders' equity	485,732	527,815	396,762	421,514	459,348

**ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

**Overview**

We are a fully integrated biopharmaceutical company that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. We currently have two marketed products in the United States, EYLEA<sup>®</sup> (aflibercept) Injection and ARCALYST<sup>®</sup> (rilonacept), and a late-stage product candidate, ZALTRAP<sup>®</sup> (aflibercept), which has been submitted for marketing approval in the United States and the European Union by our collaborator Sanofi, as described below.

In November 2011, we received U.S. marketing approval from the FDA for EYLEA<sup>®</sup> for the treatment of patients with wet AMD. Wet AMD is the leading cause of acquired blindness for people over the age of 65 in the United States and Europe. In the United States, the wet AMD market is approximately \$1.5 billion. Our net product sales of EYLEA<sup>®</sup> in the fourth quarter of 2011 were \$24.8 million. Our operating results over the next several years will be largely dependent upon our ability to successfully commercialize EYLEA<sup>®</sup> and the market penetration it achieves.

In 2011, Bayer HealthCare submitted regulatory applications for marketing approval of EYLEA<sup>®</sup> in wet AMD in the European Union, Japan, and other countries. In addition, we submitted a supplemental BLA to the FDA for marketing approval of EYLEA<sup>®</sup> in CRVO in the United States and, under PDUFA, were granted a target date for an FDA decision on our EYLEA<sup>®</sup> supplemental BLA of September 23, 2012. Bayer HealthCare also plans to submit regulatory applications in this indication in Europe in late 2012 or early 2013.

ARCALYST<sup>®</sup> (rilonacept) Injection for Subcutaneous Use is available by prescription in the United States for the treatment of CAPS, including FCAS and MWS in adults and children 12 and older. CAPS are a group of rare, inherited, auto-inflammatory conditions that afflict a small patient population. Net product sales of ARCALYST<sup>®</sup> in 2011 were \$19.9 million, and we do not expect future net product sales of ARCALYST<sup>®</sup> for the treatment of CAPS to be significant. In November 2011, the FDA accepted for review a supplemental BLA for marketing approval in the United States of ARCALYST<sup>®</sup> for the prevention of gout flares in patients initiating uric acid-lowering therapy. Under PDUFA, we were granted a target date for an FDA decision on our ARCALYST<sup>®</sup> supplemental BLA of July 30, 2012.

Sanofi submitted a regulatory application for marketing approval of ZALTRAP<sup>®</sup> for the treatment of previously-treated mCRC patients to the European Medicines Agency (EMA) in the fourth quarter of 2011, and the FDA in early February 2012.

We expect to incur substantial costs to prepare for potential commercialization of ARCALYST<sup>®</sup> for the treatment of gout flares in patients initiating uric acid-lowering therapy and ZALTRAP<sup>®</sup> for the treatment of previously-treated mCRC patients and, if one or both receive regulatory approval, to fund the launch of the product(s). Since inception, we have not generated any significant sales or profits from the commercialization of EYLEA<sup>®</sup>, ARCALYST<sup>®</sup>, or any of our other product candidates.

We have 13 product candidates in clinical development, all of which were discovered in our research laboratories. Our Trap-based, late-stage programs are:

- EYLEA<sup>®</sup>, which is being developed for the treatment of additional serious eye diseases;
- ZALTRAP<sup>®</sup>, which is being developed in oncology in collaboration with Sanofi; and
- ARCALYST<sup>®</sup>, which is being developed for the prevention of gout flares in patients initiating uric acid-lowering treatment.

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Our antibody-based clinical programs include the following fully human monoclonal antibodies:

- Sarilumab (REGN88), an antibody to the interleukin-6 receptor (IL-6R), which is being developed in rheumatoid arthritis;
- REGN727, an antibody to Proprotein Convertase Subtilisin/Kexin type 9 (PCSK9), which is being developed for low-density lipoprotein (LDL) cholesterol reduction;
- REGN668, an antibody to the interleukin-4 receptor (IL-4R), which is being developed in atopic dermatitis and eosinophilic asthma;
- REGN421, an antibody to Delta-like ligand-4 (Dll4), a novel angiogenesis target, which is being developed in oncology;
- REGN910, an antibody to Angiopoietin-2 (ANG2), another novel angiogenesis target, which is being developed in oncology;
- REGN475, an antibody to Nerve Growth Factor (NGF), which is being developed for the treatment of pain (currently on clinical hold);
- REGN728, an antibody in clinical development against an undisclosed target;
- REGN1033, an antibody in clinical development against an undisclosed target;
- REGN846, an antibody in clinical development against an undisclosed target, which is being developed in atopic dermatitis; and
- REGN1154, an antibody in clinical development against an undisclosed target.

With the exception of REGN475, REGN846, and REGN1154, which we are developing independently, all of these antibodies are being developed in collaboration with Sanofi.

Developing and commercializing new medicines entails significant risk and expense. Before significant revenues from the commercialization of our antibody candidates or new indications for our marketed products 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.

Historically, we have generally incurred net losses and negative cash flows from operations since our inception in 1988. Our potential to generate profits and positive cash flow from operations over the next several years depends significantly on our success in commercializing EYLEA<sup>®</sup>; otherwise, we expect to continue to incur operating losses. We expect to continue to incur substantial expenses related to our research and development activities, a significant portion of which we expect to be reimbursed by our collaborators. Also, our research and development activities outside our collaborations, the costs of which are not reimbursed, may expand and require additional resources. Our operating results may fluctuate from quarter to quarter and will depend on, among other factors, the net sales of our marketed products, as well as the scope and progress of our research and development efforts, the timing of certain expenses, and the amount of reimbursement that we receive from collaborators. We cannot predict whether or when ZALTRAP<sup>®</sup> or new indications for our marketed products will receive regulatory approval or, if any such approval is received, whether we will be able to successfully commercialize such product(s) and whether or when they may become profitable.

A primary driver of our expenses is our number of full-time employees. Our annual average headcount in 2011 was 1,568 compared with 1,249 in 2010 and 980 in 2009. In 2011, our average headcount increased primarily to support our expanded research and development activities in connection with our antibody collaboration with Sanofi and in connection with commercializing EYLEA<sup>®</sup> for the treatment of wet AMD. In 2012, we expect our average headcount to increase to approximately 1,800-1,850, primarily to support antibody manufacturing at our Rensselaer, New York manufacturing facilities, and activities in connection with preparing for the potential commercialization of ARCALYST<sup>®</sup> for the prevention of gout flares in patients initiating uric acid-lowering treatment.

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 2011 and 2012 to date were, and plans for the remainder of 2012 are, as follows:

**Trap-based Clinical Programs:**

**2011 and 2012 Events to Date**

**EYLEA®**

- Submitted a BLA to the U.S. FDA for the treatment of wet AMD
- FDA accepted BLA for wet AMD and granted our request for Priority Review
- FDA Advisory Committee unanimously recommended FDA approval of BLA for the treatment of wet AMD
- FDA approved EYLEA® for the treatment of wet AMD in the U.S. and product was launched
- Bayer HealthCare submitted regulatory applications for marketing approval for EYLEA® for the treatment of wet AMD in the European Union, Japan, and other countries
- Reported positive two-year data from Phase 3 VIEW 1 and VIEW 2 trials in wet AMD
- Reported positive results in the Phase 3 COPERNICUS and GALILEO trials in CRVO
- Submitted a supplemental BLA to the FDA for the treatment of CRVO
- Initiated Phase 3 trials in DME in the U.S. (VISTA) and outside the U.S. (VIVID)
- Bayer HealthCare initiated a Phase 3 trial in Asia in CNV of the retina as a result of pathologic myopia
- Bayer HealthCare initiated Phase 3 SIGHT trial in China in wet AMD

**ZALTRAP®**

- Presented positive results from the Phase 3 VELOUR trial in previously treated mCRC patients
- IDMC reviewed interim results for the Phase 3 VENICE trial in prostate cancer and recommended study continue to completion
- Reported that the VITAL trial in non-small cell lung cancer did not meet its primary endpoint
- Reported initial results in the Phase 2 AFFIRM trial in first-line mCRC
- Submitted regulatory applications for marketing approval to the EMA and FDA for the treatment of mCRC

**ARCALYST®**

- Reported positive results from two Phase 3 studies for the prevention of gout flares (PRE-SURGE 2 and RE-SURGE)
- Submitted a supplemental BLA for U.S. regulatory approval for the prevention of gout flares
- Initiated a long-term safety study for the prevention of gout flares (UPSURGE)

**2012 Plans**

- Initiate Phase 3 study in BRVO in the first quarter of 2012
- EMA decision on regulatory application for the treatment of wet AMD
- Japan authority decision on regulatory application for the treatment of wet AMD
- Target date for FDA decision on supplemental BLA for the treatment of CRVO is September 23, 2012

- Report final results in the Phase 3 VENICE trial in prostate cancer in the second quarter of 2012

- Target date for FDA decision on ARCALYST® supplemental BLA is July 30, 2012

Antibody-based Clinical Programs:

	2011 and 2012 Events to Date	2012 Plans
<b>Sarilumab</b> <i>(IL-6R Antibody)</i>	<ul style="list-style-type: none"> <li>● Reported positive Phase 2b data from the MOBILITY trial in rheumatoid arthritis</li> <li>● Reported that the Phase 2b trial in ankylosing spondylitis did not meet its primary endpoint</li> <li>● Initiated the Phase 3 stage of the Phase 2/3 MOBILITY trial</li> </ul>	<ul style="list-style-type: none"> <li>● Initiate additional Phase 3 studies</li> </ul>
<b>REGN727</b> <i>(PCSK9 Antibody)</i>	<ul style="list-style-type: none"> <li>● Initiated three Phase 2 studies for LDL cholesterol reduction</li> <li>● Reported positive initial data from two of the Phase 2 studies</li> </ul>	<ul style="list-style-type: none"> <li>● Report final data from three Phase 2 studies for LDL cholesterol reduction</li> <li>● Initiate Phase 3 program for LDL cholesterol reduction</li> </ul>
<b>REGN668</b> <i>(IL-4R Antibody)</i>	<ul style="list-style-type: none"> <li>● Initiated Phase 1b study in atopic dermatitis</li> <li>● Initiated Phase 2 proof of concept study in eosinophilic asthma</li> </ul>	<ul style="list-style-type: none"> <li>● Report initial results for Phase 1b study in atopic dermatitis and initiate Phase 2 program</li> <li>● Report initial results for Phase 2 study in eosinophilic asthma</li> </ul>
<b>REGN421</b> <i>(DII4 Antibody)</i>	<ul style="list-style-type: none"> <li>● Continued patient enrollment in Phase 1 program</li> </ul>	<ul style="list-style-type: none"> <li>● Initiate a Phase 1b program in advanced malignancies</li> </ul>
<b>REGN910</b> <i>(ANG2 Antibody)</i>	<ul style="list-style-type: none"> <li>● Continued patient enrollment in Phase 1 program</li> </ul>	
<b>REGN475</b> <i>(NGF Antibody)</i>	<ul style="list-style-type: none"> <li>● Anti-NGF class of antibodies is on clinical hold</li> <li>● Sanofi elected not to co-develop REGN475</li> </ul>	<ul style="list-style-type: none"> <li>● FDA Advisory Committee meeting scheduled for March 2012 to review safety of anti-NGF class of antibodies</li> </ul>
<b>REGN728</b> <i>(target not disclosed)</i>	<ul style="list-style-type: none"> <li>● Continued patient enrollment in Phase 1 program</li> </ul>	
<b>REGN846</b> <i>(target not disclosed)</i>	<ul style="list-style-type: none"> <li>● Continued patient enrollment in Phase 1 program</li> <li>● Sanofi elected not to co-develop REGN846</li> <li>● Initiated Phase 2a program in atopic dermatitis</li> </ul>	
<b>REGN1033</b> <i>(target not disclosed)</i>	<ul style="list-style-type: none"> <li>● IND accepted by the FDA</li> <li>● Initiated Phase 1 program</li> </ul>	

**REGN1154**  
*(target not disclosed)*

- Initiate Phase 1 program

### **Critical Accounting Policies and Use of Estimates**

A summary of the significant accounting policies that impact us is provided in Note 2 to our Financial Statements, beginning on page F-7. The preparation of financial statements in accordance with accounting principles generally accepted in the United States of America (GAAP) requires management to make estimates and assumptions that affect reported amounts and related disclosures in the financial statements. Management considers an accounting estimate to be critical if:

- It requires an assumption (or assumptions) regarding a future outcome; and
- Changes in the estimate or the use of different assumptions to prepare the estimate could have a material effect on our results of operations or financial condition.

Management believes the current assumptions used to estimate amounts reflected in our financial statements are appropriate. However, if actual experience differs from the assumptions used in estimating amounts reflected in our financial statements, the resulting changes could have a material adverse effect on our results of operations, and in certain situations, could have a material adverse effect on our liquidity and financial condition. The critical accounting estimates that impact our financial statements are described below.

### ***Revenue Recognition***

#### *Collaboration Revenue*

We earn collaboration revenue in connection with collaboration agreements to develop and commercialize product candidates and utilize our technology platforms. We currently have collaboration agreements with Sanofi and Bayer HealthCare. The terms of collaboration agreements typically include non-refundable up-front licensing payments, research progress (milestone) payments, and payments for development activities. Non-refundable up-front license payments, where continuing involvement is required of us, are deferred and recognized over the related performance period. We estimate our performance period based on the specific terms of each agreement, and adjust the performance periods, if appropriate, based on the applicable facts and circumstances. Although we did not enter into, or materially modify, any collaboration arrangements with multiple-deliverables in 2011, any future arrangements with multiple deliverables will be divided into separate units of accounting if the deliverables in the arrangement meet certain criteria, including whether the delivered item or items has value to the collaborator on a standalone basis. Payments which are based on achieving a specific performance milestone, involving a degree of risk, are recognized as revenue when the milestone is achieved and the related payment is due and non-refundable, provided there is no future service obligation associated with that milestone. Substantive performance milestones typically consist of significant achievements in the development life-cycle of the related product candidate, such as completion of clinical trials, filing for approval with regulatory agencies, and receipt of approvals by regulatory agencies. In determining whether a payment is deemed to be a substantive performance milestone, we take into consideration (i) the enhancement in value to the related development product candidate, (ii) our performance and the relative level of effort required to achieve the milestone, (iii) whether the milestone relates solely to past performance, and (iv) whether the milestone payment is considered reasonable relative to all of the deliverables and payment terms. Payments for achieving milestones which are not considered substantive are deferred and recognized over the related performance period.

We enter into collaboration agreements that include varying arrangements regarding which parties perform and bear the costs of research and development activities. We may share the costs of research and development activities with our collaborator, such as in our EYLEA® collaboration with Bayer HealthCare, or we may be reimbursed for all or a significant portion of the costs of our research and development activities, such as in our ZALTRAP® and antibody collaborations with Sanofi. We record our internal and third-party development costs associated with these collaborations as research and development expenses. When we are entitled to reimbursement of all or a portion of the research and development expenses that we incur under a collaboration, we record those reimbursable amounts as collaboration revenue proportionately as we recognize our expenses. If the collaboration is a cost-sharing arrangement in which both we and our collaborator perform development work and share costs, in periods when our collaborator incurs development expenses that benefit the collaboration and Regeneron, we also recognize, as additional research and development expense, the portion of the collaborator's development expenses that we are obligated to reimburse. In certain cases, we may also share the costs of pre-launch commercialization activities with our collaborators. We record our share of these costs as a reduction of collaboration revenue.



In connection with non-refundable licensing payments, our performance period estimates are principally based on projections of the scope, progress, and results of our research and development activities. Due to the variability in the scope of activities and length of time necessary to develop a drug product, changes to development plans as programs progress, and uncertainty in the ultimate requirements to obtain governmental approval for commercialization, revisions to performance period estimates are likely to occur periodically, and could result in material changes to the amount of revenue recognized each year in the future. In addition, our estimated performance periods may change if development programs encounter delays or we and our collaborators decide to expand or contract our clinical plans for a drug candidate in various disease indications. Also, if a collaborator terminates an agreement in accordance with the terms of the agreement, we would recognize any unamortized remainder of an up-front or previously deferred payment at the time of the termination.

#### *Product Revenue*

Product sales consist of U.S. sales of our two marketed products, EYLEA<sup>®</sup> and ARCALYST<sup>®</sup>. Revenue from product sales is recognized when persuasive evidence of an arrangement exists, title to product and associated risk of loss have passed to the customer, the price is fixed or determinable, collection from the customer is reasonably assured, we have no further performance obligations, and returns can be reasonably estimated. Our written contracts with our distributors and specialty pharmacies (collectively, our customers) stipulate that product is shipped freight on board destination (FOB destination). We record revenue from product sales upon delivery to our customers.

We sell EYLEA<sup>®</sup> in the United States to three distributors and several specialty pharmacies. We sell ARCALYST<sup>®</sup> in the United States to two specialty pharmacies. Under these distribution models, the distributors and specialty pharmacies generally take physical delivery of product. For EYLEA<sup>®</sup>, the distributors and specialty pharmacies generally sell the product directly to healthcare providers, whereas for ARCALYST<sup>®</sup>, the specialty pharmacies sell the product directly to patients.

Revenue from product sales are recorded net of applicable provisions for prompt pay discounts, rebates and chargebacks under governmental programs (including Medicaid), product returns, distribution-related fees, and other sales-related deductions. Calculating these provisions involves estimates and judgments. We review our estimates of rebates, chargebacks, and other applicable provisions each period and record any necessary adjustments in the current period's net product sales.

*Prompt Pay Discounts:* No prompt pay discounts are currently offered to our customers on sales of EYLEA<sup>®</sup>. In connection with sales of ARCALYST<sup>®</sup>, we offer discounts to our customers for prompt payments. We estimate these discounts based on customer terms and historical experience, and expect that our customers will always take advantage of this discount. Therefore, we accrue 100% of the prompt pay discount that is based on the gross amount of each ARCALYST<sup>®</sup> invoice at the time of sale. Our accrual for prompt pay discounts was not material at December 31, 2011 and 2010.

*Government Rebates and Chargebacks:* We estimate reductions to product sales for Medicaid and Veterans Administration (VA) programs, and for certain other qualifying federal and state government programs. Based upon our contracts with government agencies, statutorily-defined discounts applicable to government-funded programs, historical experience, and, in the case of EYLEA<sup>®</sup>, estimated payer mix based on third-party market research data, we estimate and record an allowance for rebates and chargebacks. Our liability for Medicaid rebates consists of estimates for claims that a state will make for a current quarter, claims for prior quarters that have been estimated for which an invoice has not been received, and invoices received for claims from prior quarters that have not been paid. Our reserves related to discounted pricing offered to VA, Public Health Services (PHS), and other institutions (collectively, qualified healthcare providers) represent our estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices we charge to our customers. Our customers charge us for the difference between what they pay for the products and the ultimate selling price to the qualified healthcare providers. Our reserve for this discounted pricing is based on expected sales to qualified healthcare providers and the chargebacks that customers have already claimed. Our government rebate and chargeback accruals were \$0.6 million at December 31, 2011, which was based on a percentage of gross sales. Government rebate and chargeback accruals were not material at December 31, 2010.

*Product Returns:* Consistent with industry practice, we offer our customers a limited right to return product purchased directly from us, which is principally based upon the product's expiration date. We will accept returns for three months prior to and up to six months after the product expiration date. Product returned is generally not resalable given the nature of our products and method of administration. We develop estimates for product returns based upon historical experience, inventory levels in the distribution channel, and other relevant factors.

We have developed estimates for EYLEA® product returns, based on several factors, including (i) our historical experience to date, and our expectation, that our customers will not stock significant supplies of EYLEA® due to contractual limitations and other mitigating circumstances, (ii) historical industry information regarding product return rates for similar specialty products, and (iii) the shelf life of the product. Estimates for ARCALYST® product returns have been developed based primarily on our historical returns experience; to date, actual ARCALYST® product returns have been negligible. We monitor product supply levels in the distribution channel, as well as sales by our customers of EYLEA® to healthcare providers and ARCALYST® to patients using product-specific data provided by our customers. If necessary, our estimates of product returns may be adjusted in the future based on actual returns experience, known or expected changes in the marketplace, or other factors. Our product returns accruals were not material at December 31, 2011 or 2010.

*Distribution-Related Fees:* We have written contracts with our customers that include terms for distribution-related fees. We estimate and record distribution and related fees due to our customers based on a percentage of gross sales. Our accrual for distribution-related fees was \$1.5 million at December 31, 2011. Our accrual for distribution-related fees at December 31, 2010 was not material.

#### *Clinical Trial Expenses*

Clinical trial costs are a significant component of research and development expenses and include costs associated with third-party contractors. We outsource a substantial portion of our clinical trial activities, utilizing external entities such as CROs, independent clinical investigators, and other third-party service providers to assist us with the execution of our clinical studies. For each clinical trial that we conduct, certain clinical trial costs are expensed immediately, while others are expensed over time based on the expected total number of patients in the trial, the rate at which patients enter the trial, and the period over which clinical investigators or CROs are expected to provide services.

Clinical activities which relate principally to clinical sites and other administrative functions to manage our clinical trials are performed primarily by CROs. CROs typically perform most of the start-up activities for our trials, including document preparation, site identification, screening and preparation, pre-study visits, training, and program management. On a budgeted basis, these start-up costs are typically 10% to 20% of the total contract value. On an actual basis, this percentage range can be significantly wider, as many of our contracts with CROs are either expanded or reduced in scope compared to the original budget, while start-up costs for the particular trial may not change materially. These start-up costs usually occur within a few months after the contract has been executed and are event driven in nature. The remaining activities and related costs, such as patient monitoring and administration, generally occur ratably throughout the life of the individual contract or study. In the event of early termination of a clinical trial, we accrue and recognize expenses in an amount based on our estimate of the remaining non-cancelable obligations associated with the winding down of the clinical trial and/or penalties.

For clinical study sites, where payments are made periodically on a per-patient basis to the institutions performing the clinical study, we accrue expense on an estimated cost-per-patient basis, based on subject enrollment and activity in each quarter. The amount of clinical study expense recognized in a quarter may vary from period to period based on the duration and progress of the study, the activities to be performed by the sites each quarter, the required level of patient enrollment, the rate at which patients actually enroll in and drop-out of the clinical study, and the number of sites involved in the study. Clinical trials that bear the greatest risk of change in estimates are typically those that have a significant number of sites, require a large number of patients, have complex patient screening requirements, and span multiple years. During the course of a trial, we adjust our rate of clinical expense recognition if actual results differ from our estimates. Our estimates and assumptions for clinical expense recognition could differ significantly from our actual results, which could cause material increases or decreases in research and development expenses in future periods when the actual results become known. No material adjustments to our past clinical trial accrual estimates were made during the years ended December 31, 2011, 2010, or 2009.

### ***Stock-based Compensation***

We recognize stock-based compensation expense for grants of stock option awards and restricted stock under our long-term incentive plans to employees and non-employee members of our board of directors based on the grant-date fair value of those awards. The grant-date fair value of an award is generally recognized as compensation expense over the award's requisite service period.

We use the Black-Scholes model to compute the estimated fair value of stock option awards. 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 historical exercise experience with previously issued employee and board of directors option grants. The expected dividend yield is zero as we have never paid dividends and do not currently anticipate paying any in the foreseeable future. Stock-based compensation expense also includes an estimate, which is made at the time of grant, of the number of awards that are expected to be forfeited. This estimate is revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

The assumptions used in computing the fair value of option awards reflect our best estimates but involve uncertainties related to market and other conditions, many of which are outside of our control. Changes in any of these assumptions may materially affect the fair value of stock options granted and the amount of stock-based compensation recognized in future periods.

In addition, we have granted performance-based stock option awards which vest based upon the optionee satisfying certain performance and service conditions as defined in the agreements. Potential compensation cost, measured on the grant date, related to these performance options will be recognized only if, and when, we estimate that these options will vest, which is based on whether we consider the options' performance conditions to be probable of attainment. Our estimates of the number of performance-based options that will vest will be revised, if necessary, in subsequent periods. Changes in these estimates may materially affect the amount of stock-based compensation that we recognize in future periods related to performance-based options.

### ***Marketable Securities***

We have invested our excess cash primarily in direct obligations of the U.S. government and its agencies, other debt securities guaranteed by the U.S. government, and money market funds that invest in U.S. government securities. We consider our marketable securities to be available-for-sale, as defined by authoritative guidance issued by the Financial Accounting Standards Board (FASB). These assets are carried at fair value and the unrealized gains and losses are included in other accumulated comprehensive income (loss) as a separate component of stockholders' equity. If the decline in the value of a marketable security in our investment portfolio is deemed to be other-than-temporary, we write down the security to its current fair value and recognize a loss that may be charged against income.

We review our portfolio of marketable securities, using both quantitative and qualitative factors, to determine if declines in fair value below cost are other-than-temporary. Such factors include the length of time and the extent to which market value has been less than cost, financial condition and near-term prospects of the issuer, recommendations of investment advisors, and forecasts of economic, market, or industry trends. With respect to debt securities, this review process also includes an evaluation of our intent to sell an individual debt security or our need to sell the debt security before its anticipated recovery or maturity. With respect to equity securities, this review process includes an evaluation of our ability and intent to hold the securities until their full value can be recovered. This review is subjective and requires a high degree of judgment. We recorded no charges for other-than-temporary impairment of our marketable securities during 2011, and inconsequential charges for other-than-temporary impairment of our marketable securities during 2010 and 2009.

**Depreciation of Property, Plant, and Equipment**

Property, plant, and equipment are stated at cost, net of accumulated depreciation. Depreciation is provided on a straight-line basis over the estimated useful lives of the assets. In some situations, the life of the asset may be extended or shortened if circumstances arise that would lead us to believe that the estimated life of the asset has changed. The life of leasehold improvements may change based on the extension of lease contracts with our landlords. Changes in the estimated lives of assets will result in an increase or decrease in the amount of depreciation recognized in future periods.

**Results of Operations****Years Ended December 31, 2011 and 2010****Net Loss**

We reported a net loss of \$221.8 million, or \$2.45 per share (basic and diluted), for the year ended December 31, 2011, compared to a net loss of \$104.5 million, or \$1.26 per share (basic and diluted) for 2010. The increase in our net loss in 2011 was principally due to higher selling, general, and administrative expenses, partly in connection with commercializing EYLEA® for wet AMD, and higher research and development expenses.

**Revenues**

Revenues in 2011 and 2010 consist of the following:

<i>(In millions)</i>	<b>2011</b>	<b>2010</b>
Collaboration revenue		
Sanofi	\$ 326.6	\$ 311.3
Bayer HealthCare	43.1	75.4
Total collaboration revenue	369.7	386.7
Net product sales	44.7	25.3
Technology licensing revenue	24.8	40.2
Contract research and other revenue	6.6	6.9
Total revenue	\$ 445.8	\$ 459.1

**Sanofi Collaboration Revenue**

The collaboration revenue we earned from Sanofi, as detailed below, consisted primarily of reimbursement for research and development expenses and recognition of revenue related to non-refundable up-front payments of \$105.0 million related to the ZALTRAP® collaboration and \$85.0 million related to the antibody collaboration.

<b>Sanofi Collaboration Revenue</b>	<b>Years ended</b>	
<i>(In millions)</i>	<b>December 31,</b>	
	<b>2011</b>	<b>2010</b>
ZALTRAP®:		
Regeneron expense reimbursement	\$ 16.9	\$ 16.5
Recognition of deferred revenue related to up-front payments	9.9	9.9
Regeneron share of ZALTRAP® commercialization expenses	(9.3)	
Total ZALTRAP®	17.5	26.4
Antibody:		
Regeneron expense reimbursement	299.3	276.0
Recognition of deferred revenue related to up-front and other payments	8.2	7.3
Recognition of revenue related to <i>VelociGene</i> ® agreement	1.6	1.6
Total antibody	309.1	284.9

Total Sanofi collaboration revenue	\$ 326.6	\$ 311.3
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Sanofi's reimbursement of our ZALTRAP® expenses increased slightly in 2011 compared to 2010, primarily due to higher costs related to manufacturing ZALTRAP® supplies, offset by a decrease in other research and development activities. Effective in 2011, we and Sanofi began equally sharing pre-launch commercialization expenses related to ZALTRAP® in accordance with the companies' collaboration agreement. Our share of these expenses was \$9.3 million in 2011, which reduced our Sanofi collaboration revenue. In connection with recognition of deferred revenue related to ZALTRAP®, as of December 31, 2011, \$22.6 million of the original \$105.0 million of up-front payments was deferred and will be recognized as revenue in future periods.

In 2011, Sanofi's reimbursement of our antibody expenses consisted of \$161.9 million under the discovery agreement and \$137.4 million of development costs under the license agreement, compared to \$137.7 million and \$138.3 million, respectively, in 2010. The higher reimbursement amount under the discovery agreement in 2011 compared to 2010 was primarily due to an increase in our antibody discovery activities. The slightly lower reimbursement of development costs in 2011 compared to 2010 was primarily due to a decrease in development activities related to REGN475, which is currently on clinical hold, offset generally by increases in development activities for other antibody candidates.

Recognition of deferred revenue related to Sanofi's \$85.0 million up-front payment and other payments increased in 2011 compared to 2010. In connection with the November 2009 amendment of the discovery agreement, Sanofi is funding up to \$30 million of agreed-upon costs incurred by us to expand our manufacturing capacity at our Rensselaer, New York facilities, of which \$28.2 million was received or receivable as of December 31, 2011. Revenue related to such funding from Sanofi is deferred and recognized as collaboration revenue prospectively over the related performance period in conjunction with the recognition of the original \$85.0 million up-front payment. As of December 31, 2011, \$76.4 million of these up-front and other payments was deferred and will be recognized as revenue in future periods.

In August 2008, we entered into a separate *VelociGene*® agreement with Sanofi. In 2011 and 2010, we recognized \$1.6 million in revenue related to this agreement.

### *Bayer HealthCare Collaboration Revenue*

The collaboration revenue we earned from Bayer HealthCare, as detailed below, consisted of cost sharing of Regeneron EYLEA® development expenses, substantive performance milestone payments, and recognition of revenue related to a non-refundable \$75.0 million up-front payment received in October 2006 and a \$20.0 million milestone payment received in August 2007 (which, for the purpose of revenue recognition, was not considered substantive).

<b>Bayer HealthCare Collaboration Revenue</b> <i>(In millions)</i>	<b>Years ended</b> <b>December 31,</b>	
	<b>2011</b>	<b>2010</b>
Cost-sharing of Regeneron EYLEA® development expenses	\$ 33.7	\$ 45.5
Substantive performance milestone payments		20.0
Recognition of deferred revenue related to up-front and other milestone payments	9.4	9.9
<b>Total Bayer HealthCare collaboration revenue</b>	<b>\$ 43.1</b>	<b>\$ 75.4</b>

Cost-sharing of our global EYLEA® development expenses with Bayer HealthCare decreased in 2011 compared to 2010 due primarily to lower clinical development costs in connection with our Phase 3 VIEW 1 trial in wet AMD and our Phase 2 trial in DME. In the fourth quarter of 2010, we earned two \$10.0 million substantive milestone payments from Bayer HealthCare for achieving positive 52-week results in the VIEW 1 study and positive 6-month results in the COPERNICUS study. Recognition of deferred revenue related to the up-front and August 2007 milestone payments from Bayer HealthCare decreased in 2011 from 2010 due to an extension of the estimated performance period over which this deferred revenue is being recognized, effective in the fourth quarter of 2011. As of December 31, 2011, \$42.4 million of these up-front and milestone payments was deferred and will be recognized as revenue in future periods.

*Net Product Sales*

Product sales consist of U.S. sales of our two marketed products, EYLEA<sup>®</sup> and ARCALYST<sup>®</sup>. We record product sales net of allowances and accruals for prompt pay discounts, rebates and chargebacks under governmental programs (including Medicaid), product returns, and distribution-related fees. We expect our customers to stock limited supplies of our products due to (i) contractual limitations that we and our customers establish, (ii) our products' specialty nature, sales price, and distribution channels, and (iii) our historical experience to date.

In November 2011, we received marketing approval from the FDA for EYLEA<sup>®</sup> for the treatment of wet AMD, at which time product sales commenced. For the year ended December 31, 2011, we recognized as revenue \$24.8 million of EYLEA<sup>®</sup> net product sales.

In 2011 and 2010, we recognized as revenue \$19.9 million and \$25.3 million, respectively, of ARCALYST<sup>®</sup> net product sales. ARCALYST<sup>®</sup> for the treatment of CAPS, a group of rare, inherited auto-inflammatory diseases that affect a very small group of people, was our first commercialized drug product. ARCALYST<sup>®</sup> net product sales in 2010 included \$20.5 million of ARCALYST<sup>®</sup> net product sales made in 2010 and \$4.8 million of previously deferred net product sales.

At December 31, 2011 and 2010, there was no deferred revenue related to net product sales.

*Technology Licensing Revenue*

In connection with our *VelocImmune*<sup>®</sup> license agreement with Astellas, the \$20.0 million non-refundable payment received in the second quarter of 2010 was deferred upon receipt and recognized as revenue ratably over the ensuing year. In addition, in connection with the amendment and extension of our license agreement with Astellas, in August 2010, we received a \$165.0 million up-front payment, which was deferred upon receipt and is being recognized as revenue ratably over a seven-year period beginning in June 2011. In connection with our *VelocImmune* license agreement with AstraZeneca, which terminated effective as of February 2011, the \$20.0 million non-refundable payment received in the first quarter of 2010 was deferred upon receipt and recognized as revenue ratably through February 2011. In 2011 and 2010, we recognized \$24.8 million and \$40.0 million, respectively, of technology licensing revenue related to these agreements. As of December 31, 2011, \$151.7 million of the August 2010 technology licensing payment received from Astellas was deferred and will be recognized as revenue in future periods.

*Contract Research and Other Revenue*

Contract research and other revenue in 2011 and 2010 included \$3.6 million and \$4.6 million, respectively, recognized in connection with our five-year grant from the NIH, which we were awarded in September 2006 as part of the NIH's Knockout Mouse Project. As of the end of 2011, no further revenue will be recognized by us in connection with this NIH Grant. In addition, under a June 2009 agreement with Novartis, we receive royalties on worldwide sales of Novartis' canakinumab. In 2011 and 2010, contract research and other revenue included \$2.3 million and \$0.7 million, respectively, of royalties from Novartis.

*Expenses*

Total operating expenses increased to \$651.0 million in 2011 from \$556.5 million in 2010. Our average headcount in 2011 increased to 1,568 from 1,249 in 2010 principally as a result of our expanding research and development activities, which were primarily attributable to our antibody collaboration with Sanofi, and 2011 activities in connection with commercializing EYLEA<sup>®</sup> in wet AMD.

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Operating expenses in 2011 and 2010 included a total of \$56.1 million and \$39.9 million, respectively, of non-cash compensation expense related to employee stock option and restricted stock awards (Non-cash Compensation Expense), as detailed below:

Expenses (In millions)	For the year ended December 31, 2011		
	Expenses before inclusion of Non-cash Compensation Expense	Non-cash Compensation Expense	Expenses as Reported
Research and development	\$ 496.7	\$ 32.8	\$ 529.5
Selling, general, and administrative	94.0	23.3	117.3
Cost of goods sold	4.2		4.2
Total operating expenses	\$ 594.9	\$ 56.1	\$ 651.0

Expenses (In millions)	For the year ended December 31, 2010		
	Expenses before inclusion of Non-cash Compensation Expense	Non-cash Compensation Expense	Expenses as Reported
Research and development	\$ 466.9	\$ 22.3	\$ 489.2
Selling, general, and administrative	47.6	17.6	65.2
Cost of goods sold	2.1		2.1
Total operating expenses	\$ 516.6	\$ 39.9	\$ 556.5

The increase in total Non-cash Compensation Expense in 2011 was primarily attributable to (i) the recognition of higher expense in 2011 in connection with performance-based stock options that we estimate will vest, (ii) the higher fair market value of our Common Stock on the date of our annual employee option grants made in December 2010 compared to recent prior years, and (iii) the recognition of higher expense related to grants of restricted stock in December 2010.

*Research and Development Expenses*

Research and development expenses increased to \$529.5 million in 2011 from \$489.2 million in 2010. The following table summarizes the major categories of our research and development expenses in 2011 and 2010:

Research and Development Expenses* (In millions)	Year Ended December 31,		Increase (Decrease)
	2011	2010	
Payroll and benefits (1)	\$ 168.9	\$ 131.7	\$ 37.2
Clinical trial expenses	67.6	86.4	(18.8)
Clinical manufacturing costs (2)	123.0	116.1	6.9
Research and other development costs	60.4	53.8	6.6
Occupancy and other operating costs	61.8	52.3	9.5
Cost-sharing of Bayer HealthCare EYLEA® development expenses (3)	47.8	48.9	(1.1)
Total research and development expenses	\$ 529.5	\$ 489.2	\$ 40.3

\* Certain prior year amounts have been reclassified to conform to the current year's presentation.



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- (1) Includes \$29.3 million and \$19.3 million of Non-cash Compensation Expense in 2011 and 2010, respectively.
- (2) Represents the full cost of manufacturing drug for use in research, preclinical development, and clinical trials, including related payroll and benefits, Non-cash Compensation Expense, manufacturing materials and supplies, drug filling, packaging, and labeling costs, depreciation, and occupancy costs of our Rensselaer manufacturing facility. Includes \$3.5 million and \$3.0 million of Non-cash Compensation Expense in 2011 and 2010, respectively.
- (3) Under our collaboration with Bayer HealthCare, in periods when Bayer HealthCare incurs EYLEA® development expenses, we also recognize, as additional research and development expense, the portion of Bayer HealthCare's EYLEA® development expenses that we are obligated to reimburse. Bayer HealthCare provides us with estimated EYLEA® development expenses for the most recent fiscal quarter. Bayer HealthCare's estimate is reconciled to its actual expenses for such quarter in the subsequent fiscal quarter and our portion of its global EYLEA® development expenses that we are obligated to reimburse is adjusted accordingly.

Payroll and benefits increased principally due to increases in employee headcount and Non-cash Compensation Expense for the reasons described above. Clinical trial expenses decreased due primarily to lower costs related to our Phase 3 clinical development program for ARCALYST® for the prevention of gout flares in patients initiated uric acid-lowering therapy, our VIEW 1 trial for EYLEA® in wet AMD, our Phase 2 trial for EYLEA® in DME, and our clinical development program for REGN475, which is currently on clinical hold, partly offset by higher costs related to our Phase 3 VISTA-DME study for EYLEA®. Clinical manufacturing costs increased primarily due to higher costs related to manufacturing supplies of EYLEA®, ZALTRAP®, and antibody candidates, partly offset by lower costs related to manufacturing clinical supplies of ARCALYST®. Research and other development costs increased primarily due to higher costs associated with our antibody programs and regulatory submissions for marketing approvals for EYLEA® in wet AMD and CRVO, and ARCALYST® for the prevention of gout flares in patients initiated uric acid-lowering therapy. Occupancy and other operating costs increased principally in connection with our higher headcount, expanded research and development activities, and new and expanded leased facilities in Tarrytown, New York. Cost-sharing of Bayer HealthCare's EYLEA® development expenses decreased primarily due to lower costs related to Bayer HealthCare's VIEW 2 trial in wet AMD, partly offset by higher costs in connection with Bayer HealthCare's Phase 3 VIVID-DME trial.

We prepare estimates of research and development costs for projects in clinical development, which include direct costs and allocations of certain costs such as indirect labor, Non-cash Compensation Expense, and manufacturing and other costs related to activities that benefit multiple projects, and, under our collaboration with Bayer HealthCare, the portion of Bayer HealthCare's EYLEA® development expenses that we are obligated to reimburse. Our estimates of research and development costs for clinical development programs are shown below:

Project Costs (In millions)	Year ended December 31,		Increase (Decrease)
	2011	2010	
ARCALYST®	\$ 43.2	\$ 56.8	\$ (13.6)
EYLEA®	147.6	138.5	9.1
ZALTRAP®	17.1	13.5	3.6
Sarilumab	27.3	25.0	2.3
REGN727	33.9	36.0	(2.1)
Other antibody candidates in clinical development	74.7	65.5	9.2
Other research programs & unallocated costs	185.7	153.9	31.8
Total research and development expenses	\$ 529.5	\$ 489.2	\$ 40.3

Drug development and approval in the United States is a multi-step process regulated by the FDA. The process begins with discovery and preclinical evaluation, leading up to the submission of an IND to the FDA which, if successful, allows the opportunity for study in humans, or clinical study, of the potential new drug. Clinical development typically involves three phases of study: Phases 1, 2, and 3. The most significant costs in clinical development are in Phase 3 clinical trials, as they tend to be the longest and largest studies in the drug development process. Following successful completion of Phase 3 clinical trials for a biological product, a BLA must be submitted to, and accepted by, the FDA, and the FDA must approve the BLA prior to commercialization of the drug. It is not uncommon for the FDA to request additional data following its review of a BLA, which can significantly increase the drug development timeline and expenses. We may elect either on our own, or at the request of the FDA, to conduct further studies that are referred to as Phase 3b and 4 studies. Phase 3b studies are initiated and either completed or substantially completed while the BLA is under FDA review. These studies are conducted under an IND. Phase 4 studies, also referred to as post-marketing studies, are studies that are initiated and conducted after the FDA has approved a product for marketing. In addition, as discovery research, preclinical development, and clinical programs progress, opportunities to expand development of drug candidates into new disease indications can emerge. We may elect to add such new disease indications to our development efforts (with the approval of our collaborator for joint development programs), thereby extending the period in which we will be developing a product. For example, we, and our collaborators where applicable, continue to explore further development of ARCALYST®, ZALTRAP®, and EYLEA® in different disease indications.

There are numerous uncertainties associated with drug development, including uncertainties related to safety and efficacy data from each phase of drug development, uncertainties related to the enrollment and performance of clinical trials, changes in regulatory requirements, changes in the competitive landscape affecting a product candidate, and other risks and uncertainties described in Item 1A, Risk Factors under Risks Related to the Development and Approval of Our Product Candidates and New Indications for Our Marketed Products, Risks Related to Commercialization of Products, and Regulatory and Litigation Risks. The lengthy process of seeking FDA approvals, and subsequent compliance with applicable statutes and regulations, require the expenditure of substantial resources. Any failure by us to obtain, or delay in obtaining, regulatory approvals could materially adversely affect our business.

For these reasons and due to the variability in the costs necessary to develop a pharmaceutical product and the uncertainties related to future indications to be studied, the estimated cost and scope of the projects, and our ultimate ability to obtain governmental approval for commercialization, accurate and meaningful estimates of the total cost to bring our product candidates to market are not available. Similarly, we are currently unable to reasonably estimate if our product candidates in clinical development will generate material product revenues and net cash inflows.

#### *Selling, General, and Administrative Expenses*

Selling, general, and administrative expenses increased to \$117.3 million in 2011 from \$65.2 million in 2010 due primarily to increases in compensation expense and recruitment costs, principally in connection with higher headcount in 2011, higher commercialization costs primarily in connection with EYLEA<sup>®</sup> for wet AMD, an increase in Non-cash Compensation Expense for the reasons described above, and higher legal expenses in connection with patent-related litigation with Genentech.

#### *Cost of Goods Sold*

Cost of goods sold increased to \$4.2 million in 2011 from \$2.1 million in 2010, due primarily to our launch of EYLEA<sup>®</sup> for the treatment of wet AMD in November 2011. Cost of goods sold in 2011 and 2010 primarily consisted of royalties and the costs of producing EYLEA<sup>®</sup> and ARCALYST<sup>®</sup> commercial supplies.

#### *Other Income and Expense*

Investment income increased to \$3.5 million in 2011 from \$2.1 million in 2010 due to higher average balances of cash and marketable securities during 2011.

Interest expense increased to \$21.3 million in 2011 from \$9.1 million in 2010. In October 2011, we issued \$400.0 million aggregate principal amount of 1.875% convertible senior notes. Total interest expense in 2011 associated with these notes, including amortization of the note discount and debt issuance costs, was \$5.4 million. In addition, interest expense includes the imputed interest portion of payments to our landlord to lease laboratory and office facilities in Tarrytown, New York, which totaled \$15.6 million in 2011 and \$9.1 million in 2010. The increase is due to our occupying in February 2011 an additional new building in Tarrytown and, therefore, we began recognizing interest expense on the related payments to our landlord.

#### *Income Tax Expense (Benefit)*

In 2011, we recognized a \$1.1 million income tax benefit, which consisted primarily of \$0.7 million related to tax legislation that allowed us to claim a refund for a portion of our unused pre-2006 research tax credits.

Years Ended December 31, 2010 and 2009**Net Loss**

Regeneron reported a net loss of \$104.5 million, or \$1.26 per share (basic and diluted), for the year ended December 31, 2010, compared to a net loss of \$67.8 million, or \$0.85 per share (basic and diluted) for 2009. The increase in our net loss in 2010 was principally due to higher research and development expenses, partly offset by higher collaboration revenue in connection with our antibody collaboration with Sanofi.

**Revenues**

Revenues in 2010 and 2009 consist of the following:

<i>(In millions)</i>	2010	2009
Collaboration revenue		
Sanofi	\$ 311.3	\$ 247.2
Bayer HealthCare	75.4	67.3
Total collaboration revenue	386.7	314.5
Net product sales	25.3	18.4
Technology licensing revenue	40.2	40.0
Contract research and other revenue	6.9	6.4
Total revenue	\$ 459.1	\$ 379.3

*Sanofi Collaboration Revenue*

The collaboration revenue we earned from Sanofi, as detailed below, consisted primarily of reimbursement for research and development expenses and recognition of revenue related to non-refundable up-front payments of \$105.0 million related to the ZALTRAP® collaboration and \$85.0 million related to the antibody collaboration.

<b>Sanofi Collaboration Revenue</b>	<b>Years ended</b>	
<i>(In millions)</i>	<b>December 31,</b>	
	<b>2010</b>	<b>2009</b>
ZALTRAP®:		
Regeneron expense reimbursement	\$ 16.5	\$ 26.6
Recognition of deferred revenue related to up-front payments	9.9	9.9
Total ZALTRAP®	26.4	36.5
Antibody:		
Regeneron expense reimbursement	276.0	198.1
Recognition of deferred revenue related to up-front and other payments	7.3	9.9
Recognition of revenue related to <i>VelociGene</i> ® agreement	1.6	2.7
Total antibody	284.9	210.7
Total Sanofi collaboration revenue	\$ 311.3	\$ 247.2

Sanofi's reimbursement of our ZALTRAP® expenses decreased in 2010 compared to 2009, primarily due to lower costs related to internal research activities and manufacturing ZALTRAP® clinical supplies.

In 2010, Sanofi's reimbursement of our antibody expenses consisted of \$137.7 million under the discovery agreement and \$138.3 million of development costs under the license agreement, compared to \$99.8 million and \$98.3 million, respectively, in 2009. The higher reimbursement amounts in 2010 compared to 2009 were due to an increase in our research activities conducted under the discovery agreement and increases in our development activities for antibody candidates under the license agreement.

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Recognition of deferred revenue related to Sanofi's \$85.0 million up-front payment decreased in 2010 compared to 2009 due to the November 2009 amendments to expand and extend the companies' antibody collaboration. In connection with the November 2009 amendment of the discovery agreement, Sanofi is funding up to \$30 million of agreed-upon costs incurred by us to expand our manufacturing capacity at our Rensselaer, New York facilities, of which \$23.4 million was received or receivable from Sanofi as of December 31, 2010. Revenue related to these payments for such funding from Sanofi is deferred and recognized as collaboration revenue prospectively over the related performance period in conjunction with the recognition of the original \$85.0 million up-front payment.

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In August 2008, we entered into a separate *VelociGene*<sup>®</sup> agreement with Sanofi. In 2010 and 2009, we recognized \$1.6 million and \$2.7 million, respectively, in revenue related to this agreement.

### *Bayer HealthCare Collaboration Revenue*

The collaboration revenue we earned from Bayer HealthCare, as detailed below, consisted of cost sharing of Regeneron EYLEA<sup>®</sup> development expenses, substantive performance milestone payments, and recognition of revenue related to a non-refundable \$75.0 million up-front payment received in October 2006 and a \$20.0 million milestone payment received in August 2007 (which, for the purpose of revenue recognition, was not considered substantive).

<b><u>Bayer HealthCare Collaboration Revenue</u></b> <i>(In millions)</i>	<b>Years ended December 31,</b>	
	<b>2010</b>	<b>2009</b>
Cost-sharing of Regeneron EYLEA <sup>®</sup> development expenses	\$ 45.5	\$ 37.4
Substantive performance milestone payments	20.0	20.0
Recognition of deferred revenue related to up-front and other milestone payments	9.9	9.9
<b>Total Bayer HealthCare collaboration revenue</b>	<b>\$ 75.4</b>	<b>\$ 67.3</b>

Cost-sharing of our EYLEA<sup>®</sup> development expenses with Bayer HealthCare increased in 2010 compared to 2009 due to higher internal development activities and higher clinical development costs in connection with our Phase 3 COPERNICUS trial in CRVO. In the fourth quarter of 2010, we earned two \$10.0 million substantive milestone payments from Bayer HealthCare for achieving positive 52-week results in the VIEW 1 study and positive 6-month results in the COPERNICUS study. In July 2009, we earned a \$20.0 million substantive performance milestone payment from Bayer HealthCare in connection with the dosing of the first patient in the COPERNICUS study.

### *Net Product Sales*

In 2010 and 2009, we recognized as revenue \$25.3 million and \$18.4 million, respectively, of ARCALYST<sup>®</sup> net product sales. We had limited historical returns experience for ARCALYST<sup>®</sup> beginning with initial sales in 2008 through the end of 2009; therefore, ARCALYST<sup>®</sup> net product sales were deferred until the right of return no longer existed and rebates could be reasonably estimated. Effective in the first quarter of 2010, we determined that we had accumulated sufficient historical data to reasonably estimate both product returns and rebates of ARCALYST<sup>®</sup>. As a result, \$4.8 million of previously deferred ARCALYST<sup>®</sup> net product sales were recognized as revenue in the first quarter of 2010. The effect of recognizing the previously deferred ARCALYST<sup>®</sup> net product sales revenue was to lower our net loss per share by \$0.06 in 2010. At December 31, 2010, there was no deferred revenue related to ARCALYST<sup>®</sup> net product sales.

### *Technology Licensing Revenue*

In connection with our *VelocImmune*<sup>®</sup> license agreements with AstraZeneca and Astellas, each of the \$20.0 million annual, non-refundable payments were deferred upon receipt and recognized as revenue ratably over approximately the ensuing year of each agreement. In both 2010 and 2009, we recognized \$40.0 million of technology licensing revenue related to these agreements. In addition, in connection with the amendment and extension of our license agreement with Astellas, in August 2010, we received a \$165.0 million up-front payment, which was deferred upon receipt and will be recognized as revenue ratably over a seven-year period beginning in June 2011.

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### *Contract Research and Other Revenue*

Contract research and other revenue in 2010 and 2009 included \$4.6 million and \$5.5 million, respectively, recognized in connection with our five-year grant from the NIH, which we were awarded in September 2006 as part of the NIH's Knockout Mouse Project.

### **Expenses**

Total operating expenses increased to \$556.5 million in 2010 from \$453.4 million in 2009. Our average headcount in 2010 increased to 1,249 from 980 in 2009 principally as a result of our expanded research and development activities, which were primarily attributable to our antibody collaboration with Sanofi.

Operating expenses in 2010 and 2009 included a total of \$39.9 million and \$31.3 million, respectively, of Non-cash Compensation Expense, as detailed below:

<u>Expenses</u> (In millions)	<b>For the year ended December 31, 2010</b>		
	<b>Expenses before inclusion of Non-cash Compensation Expense</b>		
	<b>Non-cash Compensation Expense</b>	<b>Non-cash Compensation Expense</b>	<b>Expenses as Reported</b>
Research and development	\$ 466.9	\$ 22.3	\$ 489.2
Selling, general, and administrative	47.6	17.6	65.2
Cost of goods sold	2.1		2.1
Total operating expenses	\$ 516.6	\$ 39.9	\$ 556.5

<u>Expenses</u> (In millions)	<b>For the year ended December 31, 2009</b>		
	<b>Expenses before inclusion of Non-cash Compensation Expense</b>		
	<b>Non-cash Compensation Expense</b>	<b>Non-cash Compensation Expense</b>	<b>Expenses as Reported</b>
Research and development	\$ 380.0	\$ 18.8	\$ 398.8
Selling, general, and administrative	40.4	12.5	52.9
Cost of goods sold	1.7		1.7
Total operating expenses	\$ 422.1	\$ 31.3	\$ 453.4

The increase in total Non-cash Compensation Expense in 2010 was primarily attributable to (i) the recognition of higher expense in 2010 in connection with performance-based stock options that we estimate will vest, (ii) the increase in stock option awards in 2010, due in part to the increase in headcount, and (iii) the higher fair market value of our Common Stock on the date of our annual employee option grants made in December 2009 compared to December 2008.

### *Research and Development Expenses*

Research and development expenses increased to \$489.2 million in 2010 from \$398.8 million in 2009. The following table summarizes the major categories of our research and development expenses in 2010 and 2009:

<u>Research and Development Expenses*</u>	<b>Year Ended December 31,</b>	<b>Increase</b>
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<i>(In millions)</i>	2010	2009	(Decrease)
Payroll and benefits (1)	\$ 131.7	\$ 99.9	\$ 31.8
Clinical trial expenses	86.4	98.5	(12.1)
Clinical manufacturing costs (2)	116.1	79.8	36.3
Research and other development costs	53.8	42.3	11.5
Occupancy and other operating costs	52.3	40.6	11.7
Cost-sharing of Bayer HealthCare EYLEA® development expenses (3)	48.9	37.7	11.2
Total research and development expenses	\$ 489.2	\$ 398.8	\$ 90.4



\* Certain prior year amounts have been reclassified to conform to the current year's presentation.

- (1) Includes \$19.3 million and \$16.2 million of Non-cash Compensation Expense in 2010 and 2009, respectively.
- (2) Represents the full cost of manufacturing drug for use in research, preclinical development, and clinical trials, including related payroll and benefits, Non-cash Compensation Expense, manufacturing materials and supplies, drug filling, packaging, and labeling costs, depreciation, and occupancy costs of our Rensselaer manufacturing facility. Includes \$3.0 million and \$2.6 million of Non-cash Compensation Expense in 2010 and 2009, respectively.
- (3) Under our collaboration with Bayer HealthCare, in periods when Bayer HealthCare incurs EYLEA® development expenses, we also recognize, as additional research and development expense, the portion of Bayer HealthCare's EYLEA® development expenses that we are obligated to reimburse. Bayer HealthCare provides us with estimated EYLEA® development expenses for the most recent fiscal quarter. Bayer HealthCare's estimate is reconciled to its actual expenses for such quarter in the subsequent fiscal quarter and our portion of its global EYLEA® development expenses that we are obligated to reimburse is adjusted accordingly.

Payroll and benefits increased principally due to the increase in employee headcount, as described above. Clinical trial expenses decreased due primarily to lower costs related to our Phase 3 clinical development program for ARCALYST® in gout, partly offset by higher costs related to our clinical development programs for EYLEA®, principally in connection with our COPERNICUS trial in CRVO. Clinical manufacturing costs increased due to higher facility-related costs in connection with the expansion of our manufacturing capacity at our Rensselaer facility and higher costs related to manufacturing clinical supplies of monoclonal antibodies, partly offset by lower costs related to manufacturing ZALTRAP® clinical supplies. Research and other development costs increased primarily due to higher costs associated with our antibody programs. Occupancy and other operating costs increased principally in connection with our higher headcount, expanded research and development activities, and new and expanded leased laboratory and office facilities in Tarrytown, New York. Cost-sharing of Bayer HealthCare's EYLEA® development expenses increased primarily due to higher costs in connection with Bayer HealthCare's VIEW 2 trial in wet AMD.

We prepare estimates of research and development costs for projects in clinical development, which include direct costs and allocations of certain costs such as indirect labor, Non-cash Compensation Expense, and manufacturing and other costs related to activities that benefit multiple projects, and, under our collaboration with Bayer HealthCare, the portion of Bayer HealthCare's EYLEA® development expenses that we are obligated to reimburse. Our estimates of research and development costs for clinical development programs are shown below:

<b>Project Costs</b> <i>(In millions)</i>	<b>Year ended</b> <b>December 31,</b>		<b>Increase</b>
	<b>2010</b>	<b>2009</b>	<b>(Decrease)</b>
ARCALYST®	\$ 56.8	\$ 67.7	\$ (10.9)
EYLEA®	138.5	109.8	28.7
ZALTRAP®	13.5	23.3	(9.8)
Sarilumab	25.0	36.9	(11.9)
REGN727	36.0	21.1	14.9
Other antibody candidates in clinical development	65.5	53.3	12.2
Other research programs & unallocated costs	153.9	86.7	67.2
Total research and development expenses	\$ 489.2	\$ 398.8	\$ 90.4

For the reasons described above under Research and Development Expenses for the years ended December 31, 2011 and 2010, and due to the variability in the costs necessary to develop a pharmaceutical product and the uncertainties related to future indications to be studied, the estimated cost and scope of the projects, and our ultimate ability to obtain governmental approval for commercialization, accurate and meaningful estimates of the total cost to bring our product candidates to market are not available. Similarly, we are currently unable to reasonably estimate if our product candidates in clinical development will generate material product revenues and net cash inflows.

#### *Selling, General, and Administrative Expenses*

Selling, general, and administrative expenses increased to \$65.2 million in 2010 from \$52.9 million in 2009 due primarily to increases in compensation expense and recruitment costs, principally in connection with higher headcount in 2010, and an increase in Non-cash Compensation Expense for the reasons described above.

*Cost of Goods Sold*

Cost of goods sold in 2010 and 2009 was \$2.1 million and \$1.7 million, respectively, and consisted primarily of royalties and other period costs related to ARCALYST® commercial supplies. During 2010 and 2009, ARCALYST® shipments to our customers primarily consisted of supplies of inventory manufactured and expensed as research and development costs prior to FDA approval in 2008; therefore, the costs of these supplies were not included in costs of goods sold.

*Other Income and Expense*

Investment income decreased to \$2.1 million in 2010 from \$4.5 million in 2009, due primarily to lower yields on, and lower average balances of, cash and marketable securities.

Interest expense increased to \$9.1 million in 2010 from \$2.3 million in 2009. Interest expense is primarily attributable to the imputed interest portion of payments to our landlord, commencing in the third quarter of 2009, to lease newly constructed laboratory and office facilities in Tarrytown, New York.

*Income Tax Expense (Benefit)*

In 2010, we did not recognize any income tax expense or benefit. In 2009, we recognized a \$4.1 million income tax benefit, consisting primarily of (i) \$2.7 million resulting from tax legislation that allowed us to claim a refund of U.S. federal alternative minimum tax that we paid in 2008, and (ii) \$0.7 million resulting from tax legislation that allowed us to claim a refund for a portion of our unused pre-2006 research tax credits.

**Liquidity and Capital Resources**

Since our inception in 1988, we have financed our operations primarily through offerings of our equity securities, private placements of convertible debt, purchases of our equity securities by our collaborators, including Sanofi, revenue earned under our past and present research and development agreements, including our agreements with Sanofi and Bayer HealthCare, EYLEA® and ARCALYST® product revenue, our technology licensing agreements, our past contract manufacturing agreements, and investment income.

*Sources and Uses of Cash for the Years Ended December 31, 2011, 2010, and 2009*

At December 31, 2011, we had \$810.6 million in cash, cash equivalents, and marketable securities (including \$7.7 million of restricted cash and marketable securities) compared with \$626.9 million at December 31, 2010 (including \$7.5 million of restricted cash and marketable securities) and \$390.0 million (including \$1.6 million of restricted cash) at December 31, 2009. In October 2011, we completed a private placement of \$400.0 million aggregate principal amount of 1.875% convertible senior notes and received net proceeds of approximately \$391.1 million after deducting the initial purchaser's discount and issuance costs. In connection with the offering of the convertible senior notes, we entered into convertible note hedge and warrant transactions, which had a net cost to us of \$23.7 million. In October 2010, we completed an underwritten public offering of 6,325,000 shares of Common Stock and received net proceeds of \$174.8 million. In connection with the July 2010 amendment and extension of our non-exclusive license agreement with Astellas, we received a \$165.0 million up-front payment from Astellas in August 2010.

*Cash (Used in) Provided by Operations*

Net cash used in operations was \$141.7 million in 2011 and \$69.9 million in 2009, and net cash provided by operations was \$99.2 million in 2010. Our net losses of \$221.8 million in 2011, \$104.5 million in 2010, and \$67.8 million in 2009 included \$56.1 million, \$39.9 million, and \$31.3 million, respectively, of Non-cash Compensation Expense. Our net losses also included depreciation and amortization of \$31.1 million, \$19.7 million, and \$14.2 million in 2011, 2010, and 2009, respectively.

At December 31, 2011, Sanofi and trade accounts receivable increased by \$21.1 million, compared to end-of-year 2010, primarily due to EYLEA<sup>®</sup> product sales, which commenced in November 2011. Due to the payment terms granted to our customers, our EYLEA<sup>®</sup> product sales in 2011, generally, had not yet been collected as of December 31, 2011. Our deferred revenue at December 31, 2011 decreased by \$40.3 million, compared to end-of-year 2010, primarily due to (i) amortization of the \$165.0 million up-front payment from Astellas, as described above, which was initially deferred and is being recognized ratably over the seven-year period that commenced in mid-2011, and (ii) amortization of previously deferred payments under our Sanofi and Bayer HealthCare collaborations. Accounts payable, accrued expenses, and other liabilities increased \$50.0 million at December 31, 2011, compared to end-of-year 2010, primarily in connection with (i) higher payroll-related liabilities, due in part to funding payment of our year-end 2010 employee cash bonuses prior to December 31, 2010 whereas year-end 2011 employee cash bonuses were funded subsequent to December 31, 2011 and (ii) our expanded levels of activities and expenditures, partly in connection with EYLEA<sup>®</sup> commercialization activities.

At December 31, 2010, Sanofi and trade accounts receivable increased by \$17.5 million, compared to end-of-year 2009, primarily due to a higher receivable balance related to our antibody collaboration with Sanofi. Our deferred revenue at December 31, 2010 increased by \$158.2 million, compared to end-of-year 2009, primarily due to (i) the receipt of the \$165.0 million up-front payment from Astellas, as described above, which was deferred, and (ii) Sanofi's funding of \$22.9 million of agreed-upon costs incurred by us during 2010 to expand our manufacturing capacity at our Rensselaer facilities, which was deferred and is being recognized as collaboration revenue prospectively over the related performance period in conjunction with the original \$85.0 million up-front payment received from Sanofi. These increases were partly offset by amortization of previously received deferred payments under our Sanofi and Bayer HealthCare collaborations.

At December 31, 2009, Sanofi and trade accounts receivable increased by \$30.5 million, compared to end-of-year 2008, primarily due to a higher receivable balance related to our antibody collaboration with Sanofi. Our deferred revenue at December 31, 2009 decreased by \$27.5 million, compared to end-of-year 2008, primarily due to the amortization of previously received deferred payments under our collaborations with Sanofi and Bayer HealthCare. Accounts payable, accrued expenses, and other liabilities increased \$12.6 million at December 31, 2009, compared to end-of-year 2008, primarily in connection with our expanded levels of activities and expenditures, including higher liabilities for clinical-related expenses, which were partly offset by an \$8.6 million decrease in the cost-sharing payment due to Bayer HealthCare in connection with our EYLEA<sup>®</sup> collaboration.

#### *Cash Provided by (Used in) Investing Activities*

Net cash provided by investing activities was \$128.5 million in 2011, compared with net cash used in investing activities of \$437.0 million and \$2.1 million in 2010 and 2009, respectively. Sales or maturities of marketable securities exceeded purchases by \$186.0 million in 2011 and \$95.1 million in 2009. In 2010, purchases of marketable securities exceeded sales or maturities by \$331.4 million. Capital expenditures of \$57.2 million, \$99.7 million, and \$97.3 million in 2011, 2010, and 2009, respectively, included costs in connection with expanding our manufacturing capacity at our Rensselaer, New York facilities and tenant improvements and related costs in connection with our leased facilities in Tarrytown, New York.

#### *Cash Provided by Financing Activities*

Net cash provided by financing activities was \$384.2 million in 2011, \$243.3 million in 2010 and \$31.4 million in 2009. As described above, in October 2011, we completed a private placement of convertible senior notes and received net proceeds of \$391.1 million, and entered into convertible note hedge and warrant transactions, which had a net cost to us of \$23.7 million. Also as described above, in October 2010, we completed an offering of our Common Stock and received net proceeds of \$174.8 million. In addition, net proceeds from issuances of Common Stock in connection with exercises of stock options were \$18.5 million in 2011, \$22.0 million in 2010, and \$8.6 million in 2009. In 2010 and 2009, we received \$47.5 million and \$23.6 million, respectively, of tenant improvement reimbursements from our landlord in connection with our Tarrytown facilities, which we are deemed to own in accordance with FASB authoritative guidance.

**Fair Value of Marketable Securities**

At December 31, 2011 and 2010, we held marketable securities whose aggregate fair value totaled \$325.2 million and \$513.9 million, respectively. The composition of our portfolio of marketable securities on these dates was as follows:

<b>Investment type</b>	<b>2011</b>		<b>2010</b>	
	<b>Fair Value</b>	<b>Percent</b>	<b>Fair Value</b>	<b>Percent</b>
<b>Unrestricted</b>				
U.S. government obligations	\$ 284.9	87%	\$ 434.4	85%
U.S. government guaranteed corporate bonds	15.3	5%	64.0	13%
Municipal bonds	15.3	5%	1.6	
Equity securities	3.0	1%	3.6	1%
U.S. government guaranteed collateralized mortgage obligations	0.6		2.1	
Mortgage-backed securities	0.1		1.1	
Total unrestricted marketable securities	319.2	98%	506.8	99%
<b>Restricted</b>				
U.S. government obligations	6.0	2%	7.1	1%
Total marketable securities	\$ 325.2	100 %	\$ 513.9	100 %

In addition, at December 31, 2011 and 2010, we had \$485.4 million and \$113.0 million, respectively, of cash, cash equivalents, and restricted cash, primarily held in money market funds that invest in U.S. government securities.

We classify our investments using a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value. The three tiers are Level 1, defined as observable inputs such as quoted prices in active markets; Level 2, defined as inputs other than quoted prices in active markets that are either directly or indirectly observable; and Level 3, defined as unobservable inputs in which little or no market data exists, therefore requiring an entity to develop its own assumptions. Our methods for valuing our marketable securities are described in Note 6 to our financial statements included in this Annual Report on Form 10-K.

We held one Level 3 marketable security, which had no fair value at December 31, 2011 and 2010. This Level 3 security was valued using information provided by our investment advisors and other sources, including quoted bid prices which took into consideration the securities' lack of liquidity. During the year ended December 31, 2009, we recorded charges for other-than-temporary impairment of this Level 3 marketable security totaling \$0.1 million; therefore, as of December 31, 2009, the fair value of this security had been written down to zero. There were no purchases, sales, or maturities of Level 3 marketable securities and no unrealized gains or losses related to Level 3 marketable securities for the years ended December 31, 2011 and 2010. There were no transfers of marketable securities between Levels 1, 2, or 3 classifications during the years ended December 31, 2011 and 2010.

**Collaborations with Sanofi****ZALTRAP®(afibercept)**

In September 2003, we entered into a collaboration agreement with Aventis Pharmaceuticals Inc. (predecessor to Sanofi U.S.) to collaborate on the development and commercialization of ZALTRAP® in all countries other than Japan, where we retained the exclusive right to develop and commercialize ZALTRAP®. Sanofi 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.

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In January 2005, we and Sanofi amended the collaboration agreement to exclude, from the scope of the collaboration, the development and commercialization of ZALTRAP<sup>®</sup> for intraocular delivery to the eye. In connection with this amendment, Sanofi made a \$25.0 million non-refundable payment to us.

In December 2005, we and Sanofi amended our collaboration agreement to expand the territory in which the companies are collaborating on the development of ZALTRAP<sup>®</sup> to include Japan. In connection with this amendment, Sanofi 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 will share co-promotion rights and profits on sales, if any, of ZALTRAP<sup>®</sup> outside of Japan for disease indications included in our collaboration. In Japan, we are entitled to a royalty of approximately 35% on annual sales of ZALTRAP<sup>®</sup>. We may also receive up to \$400 million in substantive milestone payments upon receipt of specified marketing approvals, including up to \$360 million in milestone payments related to the receipt of marketing approvals for up to eight ZALTRAP<sup>®</sup> oncology and other indications in the United States or the European Union and up to \$40 million related to the receipt of marketing approvals for up to five ZALTRAP<sup>®</sup> oncology indications in Japan.

We have agreed to manufacture clinical supplies of ZALTRAP<sup>®</sup> at our plant in Rensselaer, New York. Sanofi has agreed to be responsible for providing commercial scale manufacturing capacity for ZALTRAP<sup>®</sup>.

Under the collaboration agreement, as amended, agreed-upon worldwide ZALTRAP<sup>®</sup> 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. If the collaboration becomes profitable, we will be obligated to reimburse Sanofi for 50% of these 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. Since inception of the collaboration agreement through December 31, 2011, we and Sanofi have incurred \$763.4 million in agreed-upon development expenses related to ZALTRAP<sup>®</sup>. If the collaboration becomes profitable, we will also be obligated to reimburse Sanofi for 50% of the \$25.0 million payment received in connection with the January 2005 amendment to our collaboration agreement. In addition, if the first commercial sale of an aflibercept product for intraocular delivery to the eye predates the first commercial sale of a ZALTRAP<sup>®</sup> product under the collaboration by two years, we will begin reimbursing Sanofi for up to \$7.5 million of ZALTRAP<sup>®</sup> development expenses in accordance with a formula until the first commercial ZALTRAP<sup>®</sup> sale under the collaboration occurs. As described above under Item 1. Business Clinical Programs, based upon the positive findings in the Phase 3 VELOUR study, Sanofi has submitted a regulatory application for marketing approval of ZALTRAP<sup>®</sup> for the treatment of previously-treated mCRC patients to the EMA in the fourth quarter of 2011 and the FDA in February 2012. In addition, the Phase 3 VENICE study for the first-line treatment for hormone-refractory metastatic prostate cancer in combination with docetaxel/prednisone is ongoing.

Sanofi funded \$16.9 million, \$16.5 million, and \$26.6 million, respectively, of our ZALTRAP<sup>®</sup> development costs in 2011, 2010, and 2009. In addition, in 2011, we and Sanofi began equally sharing ZALTRAP<sup>®</sup> pre-launch commercialization expenses under the collaboration agreement; as a result, we funded \$9.3 million of Sanofi's ZALTRAP<sup>®</sup> pre-launch commercialization expenses in 2011. At December 31, 2011, there was a net payable of \$3.7 million to Sanofi in connection with the companies' ZALTRAP<sup>®</sup> collaboration, and at December 31, 2010 and 2009, amounts receivable from Sanofi in connection with the ZALTRAP<sup>®</sup> collaboration were \$3.9 million and \$3.6 million, respectively. In addition, the up-front payments from Sanofi of \$80.0 million in September 2003 and \$25.0 million in January 2006 were recorded to deferred revenue and are being recognized as contract research and development revenue over the period during which we expect to perform services. In 2011, 2010, and 2009, we recognized \$9.9 million per year of revenue, respectively, related to these up-front payments.

Sanofi 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 for 50% of ZALTRAP<sup>®</sup> development expenses will terminate and we will retain all rights to ZALTRAP<sup>®</sup>.

### *Antibodies*

In November 2007, we and Sanofi entered into a global, strategic collaboration to discover, develop, and commercialize fully human monoclonal antibodies. The collaboration is governed by a Discovery and Preclinical Development Agreement and a License and Collaboration Agreement. In connection with the execution of the discovery agreement in 2007, we received a non-refundable up-front payment of \$85.0 million from Sanofi. Pursuant to the collaboration, Sanofi is funding our research to identify and validate potential drug discovery targets and

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develop fully human monoclonal antibodies against these targets. In November 2009, we and Sanofi amended these collaboration agreements to expand and extend our antibody collaboration. Under the amended discovery agreement, Sanofi agreed to fund up to \$160 million per year of our antibody discovery activities in 2010 through 2017, subject to a one-time option for Sanofi to adjust the maximum reimbursement amount down to \$120 million per year commencing in 2014 if over the prior two years certain specified criteria were not satisfied. In 2010, as we scaled up our capacity to conduct antibody discovery activities, Sanofi funded \$137.7 million of our preclinical research under the amended discovery agreement. The balance between that amount and \$160 million, or \$22.3 million, has been added to the funding otherwise available to us in 2011-2012 under the amended discovery agreement. The amended discovery agreement will expire on December 31, 2017; however, Sanofi has an option to extend the agreement for up to an additional three years for further antibody development and preclinical activities.

For each drug candidate identified through discovery research under the discovery agreement, Sanofi has the option to license rights to the candidate under the license agreement. If it elects to do so, Sanofi will co-develop the drug candidate with us through product approval. Under certain defined circumstances, upon exercising its option to license rights to particular candidates, Sanofi must make a \$10 million substantive milestone payment to us. Under the license agreement, agreed upon worldwide development expenses incurred by both companies during the term of the agreement are funded by Sanofi, except that following receipt of the first positive Phase 3 trial results for a co-developed drug candidate, subsequent Phase 3 trial-related costs for that drug candidate (called Shared Phase 3 Trial Costs) are shared 80% by Sanofi and 20% by us. If the collaboration becomes profitable, we will be obligated to reimburse Sanofi for 50% of development expenses that were fully funded by Sanofi (or half of \$582.3 million as of December 31, 2011) and 30% of Shared Phase 3 Trial Costs, in accordance with a defined formula based on the amounts of these expenses and our share of the collaboration profits from commercialization of collaboration products. However, we are not required to apply more than 10% of our share of the profits from collaboration products in any calendar quarter towards reimbursing Sanofi for these development costs. If Sanofi does not exercise its option to license rights to a particular drug candidate under the license agreement, we retain the exclusive right to develop and commercialize such drug candidate, and Sanofi will receive a royalty on sales, if any.

Sanofi will lead commercialization activities for products developed under the license agreement, subject to our right to co-promote such products. The parties will equally share profits and losses from sales within the United States. The parties will share profits outside the United States on a sliding scale based on sales starting at 65% (Sanofi)/35% (us) and ending at 55% (Sanofi)/45% (us), and losses outside the United States at 55% (Sanofi)/45% (us). In addition to profit sharing, we are entitled to receive up to \$250 million in sales milestone payments, with milestone payments commencing only if and after aggregate annual sales outside the United States exceed \$1.0 billion on a rolling 12-month basis.

We are obligated to use commercially reasonable efforts to supply clinical requirements of each drug candidate under the collaboration until commercial supplies of that drug candidate are being manufactured. In connection with the November 2009 amendment of the collaboration's discovery agreement, Sanofi is funding up to \$30 million of agreed-upon costs incurred by us to expand our manufacturing capacity at our Rensselaer, New York facilities, of which \$28.2 million was received or receivable as of December 31, 2011.

In 2011, 2010, and 2009, Sanofi funded \$161.9 million, \$137.7 million, and \$99.8 million, respectively, of our expenses under the collaboration's discovery agreement and \$137.4 million, \$138.3 million, and \$98.3 million, respectively, of our development costs under the license agreement. Of these amounts, \$75.6 million, \$73.4 million and \$57.9 million were included in accounts receivable as of December 31, 2011, 2010, and 2009, respectively. The \$85.0 million up-front payment received from Sanofi in December 2007 was recorded to deferred revenue and is being recognized as collaboration revenue over the period during which we expect to perform services. In addition, reimbursements by Sanofi of our costs to expand our manufacturing capacity are recorded to deferred revenue and recognized prospectively as collaboration revenue over the same period applicable to recognition of the \$85.0 million up-front payment. In 2011, 2010, and 2009, we recognized \$8.2 million, \$7.3 million, and \$9.9 million of revenue, respectively, related to these deferred payments.

In connection with the antibody collaboration, in August 2008, we entered into a separate agreement with Sanofi to use our proprietary *VelociGene*<sup>®</sup> technology platform to supply Sanofi with genetically modified mammalian models of gene function and disease. The agreement provides for minimum annual order quantities for the term of the agreement, which extends through December 2012, for which we expect to receive payments totaling a minimum of \$21.5 million, of which \$12.7 million had been received as of December 31, 2011.

With respect to each antibody product which enters development under the license agreement, Sanofi or we may, by giving twelve months notice, opt-out of further development and/or commercialization of the product, in which event the other party retains exclusive rights to continue the development and/or commercialization of the product. We may also opt-out of the further development of an antibody product if we give notice to Sanofi within thirty days of the date that Sanofi elects to jointly develop such antibody product under the license agreement. Each of the discovery agreement and the license agreement contains other termination provisions, including for material breach by the other party. Prior to December 31, 2017, Sanofi has the right to terminate the amended discovery agreement without cause with at least three months advance written notice; however, except under defined circumstances, Sanofi would be obligated to immediately pay to us the full amount of unpaid research funding during the remaining term of the research agreement through December 31, 2017. Upon termination of the collaboration in its entirety, our obligation to reimburse Sanofi for development costs out of any future profits from collaboration products will terminate.

In December 2007, we sold Sanofi 12 million newly issued, unregistered shares of Common Stock at an aggregate cash price of \$312.0 million, or \$26.00 per share of Common Stock. As a condition to the closing of this transaction, Sanofi entered into an investor agreement with us. This agreement, which was amended in November 2009, contains certain demand rights, stand-still provisions, and other restrictions, which are more fully described in Note 13 to our Financial Statements. In addition, in October 2010, Sanofi purchased 1,017,401 shares of Common Stock in our underwritten public offering.

#### ***Collaboration with Bayer HealthCare***

In October 2006, we entered into a license and collaboration agreement with Bayer HealthCare to globally develop, and commercialize outside the United States, EYLEA<sup>®</sup>. Under the terms of the agreement, Bayer HealthCare made a non-refundable up-front payment to us of \$75.0 million. In August 2007, we received a \$20.0 million milestone payment (which, for the purpose of revenue recognition, was not considered substantive) from Bayer HealthCare following dosing of the first patient in the VIEW 1 study of EYLEA<sup>®</sup> in wet AMD. In July 2009, we received a \$20.0 million substantive performance milestone payment from Bayer HealthCare following dosing of the first patient in the COPERNICUS study of EYLEA<sup>®</sup> in CRVO. In both December 2010 and January 2011, we received a \$10.0 million substantive milestone payment (for a total of \$20.0 million) from Bayer HealthCare for achieving positive 52-week results in the VIEW 1 study and positive 6-month results in the COPERNICUS study, respectively. We are eligible to receive up to \$50 million in future substantive milestone payments related to marketing approvals of EYLEA<sup>®</sup> in major market countries outside the United States. We are also eligible to receive up to \$135 million in sales milestone payments if total annual sales of EYLEA<sup>®</sup> outside the United States achieve certain specified levels starting at \$200 million.

We will share equally with Bayer HealthCare in any future profits arising from the commercialization of EYLEA<sup>®</sup> outside the United States. If EYLEA<sup>®</sup> 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 HealthCare out of our share of the collaboration profits for 50% of the agreed-upon development expenses that Bayer HealthCare has incurred (or half of \$370.9 million at December 31, 2011) in accordance with a formula based on the amount of development expenses that Bayer HealthCare 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 commercialization of EYLEA<sup>®</sup> and retain exclusive rights to any future profits from such commercialization in the United States. In June 2011, Bayer HealthCare submitted regulatory applications for marketing approval of EYLEA<sup>®</sup> in wet AMD in the European Union, Japan, and other countries. We and Bayer HealthCare continue to evaluate EYLEA<sup>®</sup> in certain Phase 3 programs in patients with wet AMD, and are evaluating EYLEA<sup>®</sup> in Phase 3 programs in patients with CRVO, DME, and CNV of the retina as a result of pathologic myopia. We are also obligated to use commercially reasonable efforts to supply clinical and commercial product requirements.

The \$75.0 million up-front payment and the \$20.0 million milestone payment received in August 2007 from Bayer HealthCare were recorded to deferred revenue. In 2011, 2010, and 2009, we recognized \$9.4 million, \$9.9 million, and \$9.9 million, respectively, of revenue related to these payments. The \$10.0 million substantive milestone payments received from Bayer HealthCare in each of December 2010 and January 2011 were recognized as collaboration revenue in 2010, and the \$20.0 million substantive performance milestone payment received from Bayer HealthCare in July 2009 was recognized as collaboration revenue in 2009.



Under the terms of the agreement, in 2009 and thereafter, all agreed upon EYLEA® development expenses incurred by both companies under a global development plan will be shared equally. Primarily in connection with sharing development expenses in 2011, 2010, and 2009, net amounts paid or payable to Bayer HealthCare were \$8.3 million, \$2.6 million, and \$0.3 million, respectively. At December 31, 2011, \$4.5 million was receivable from Bayer HealthCare, and at December 31, 2010, \$2.3 million was payable to Bayer HealthCare, in connection with cost-sharing of EYLEA® expenses under the collaboration.

Bayer HealthCare 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 EYLEA®.

#### ***License Agreement with Astellas***

Under this non-exclusive license agreement, Astellas made a \$20.0 million annual, non-refundable payment to us in each of 2010, 2009, 2008, and 2007. In July 2010, the license agreement with Astellas was amended and extended through June 2023. Under the terms of the amended agreement, Astellas made a \$165.0 million up-front payment to us in August 2010. In addition, Astellas will make a \$130.0 million second payment to us in June 2018 unless the license agreement has been terminated prior to that date. Astellas has the right to terminate the agreement at any time by providing 90 days advance written notice. Under certain limited circumstances, such as our material breach of the agreement, Astellas may terminate the agreement and receive a refund of a portion of its up-front payment or, if such termination occurs after June 2018, a portion of its second payment, to us under the July 2010 amendment to the agreement. We are entitled to receive a mid-single digit royalty on any future sales of antibody products discovered by Astellas using our *VelocImmune*® technology.

#### ***License Agreement with AstraZeneca***

Under this non-exclusive license agreement, AstraZeneca made a \$20.0 million annual, non-refundable payment to us in each of 2010, 2009, 2008, and 2007. In November 2010, as permitted by the agreement, MedImmune Limited (as successor by novation from AstraZeneca) gave written notice of voluntary termination of the agreement, effective in February 2011. We remain entitled to receive mid-single digit royalties on any future sales of antibody products discovered by MedImmune using our *VelocImmune*® technology.

#### ***National Institutes of Health Grant***

Under our five-year grant from the NIH, as amended, we were entitled to receive a minimum of \$25.3 million over the five-year period beginning in September 2006, subject to compliance with the grant's terms and annual funding approvals, including \$1.5 million to optimize our existing C57BL/6 ES cell line and its proprietary growth medium. In 2011, 2010, and 2009, we earned \$3.6 million, \$4.6 million, and \$5.5 million, respectively, of funding under the NIH Grant, of which \$0.4 million and \$1.0 million, respectively, was receivable at the end of 2011 and 2010. Other than the amount receivable at the end of 2011, no further funding will be received by us in connection with the NIH Grant.

#### ***License Agreement with Collectis***

In July 2008, we and Collectis S.A. entered into an Amended and Restated Non-Exclusive License Agreement. The amended license agreement resolved a dispute between the parties related to the interpretation of a license agreement entered into by the parties in December 2003 pursuant to which we licensed certain patents and patent applications relating to a process for the specific replacement of a copy of a gene in the receiver genome by homologous recombination. Pursuant to the amended license agreement, in July 2008, we made a non-refundable \$12.5 million payment to Collectis and agreed to pay Collectis a low single-digit royalty based on revenue received by us from any future licenses or sales of our *VelociGene*® or *VelocImmune*® products and services. No royalties are payable to Collectis with respect to our *VelocImmune*® license agreements with AstraZeneca and Astellas or our antibody collaboration with Sanofi. In addition, no royalties are payable to Collectis on any revenue from commercial sales of antibodies from our *VelocImmune*® technology. We are amortizing our \$12.5 million payment to Collectis in proportion to past and anticipated future revenues under our license agreements with AstraZeneca and Astellas and our antibody discovery agreement with Sanofi (as amended in November 2009).

***License and Partial Settlement Agreement with Genentech***

In December 2011, we and Genentech entered into a Non-Exclusive License and Partial Settlement Agreement relating to ophthalmic sales of EYLEA<sup>®</sup> in the United States. Pursuant to the agreement, we received a non-exclusive license to certain patents relating to VEGF receptor proteins, known as the Davis-Smyth patents, and other technology patents. The Davis-Smyth patents are the subject of patent litigation between us and Genentech now pending in the United States District Court, Southern District of New York. Patent litigation is continuing with respect to matters not covered by the Genentech Agreement (see Item 3. Legal Proceedings ).

Under the terms of the agreement with Genentech, we agreed to make payments to Genentech based on U.S. sales of EYLEA<sup>®</sup> commencing upon FDA approval of EYLEA<sup>®</sup> in November 2011 through May 7, 2016. We will be required to make a one-time, non-refundable \$60 million payment upon cumulative U.S. sales of EYLEA<sup>®</sup> reaching \$400 million. In addition, we agreed to pay royalties of 4.75% on cumulative U.S. sales of EYLEA<sup>®</sup> between \$400 million and \$3 billion and 5.5% on any cumulative U.S sales of EYLEA<sup>®</sup> over \$3 billion. As we record net product sales of EYLEA<sup>®</sup>, we are recognizing expense in connection with the Genentech Agreement using a blended mid-single digit royalty rate that reflects both the \$60 million payment and the royalties payable on cumulative sales and that is based upon our estimate of cumulative EYLEA<sup>®</sup> sales through May 7, 2016.

***Lease Tarrytown, New York Facilities***

We lease approximately 553,000 square feet of laboratory and office space at facilities in Tarrytown, New York, under a December 2006 lease agreement, as amended. These facilities include approximately 230,000 square feet of newly constructed space in two new buildings (Buildings A and B) that were completed during the third quarter of 2009 and approximately 131,000 square feet of additional new space in a third new building (Building C), that was completed in early 2011. The lease will expire in June 2024 and contains three renewal options to extend the term of the lease by five years each, as well as early termination options on approximately 323,000 square feet of space. The lease provides for monthly payments over its term and additional charges for utilities, taxes, and operating expenses. In connection with the lease, we have issued a \$3.4 million letter of credit to our landlord, which is fully collateralized by cash and marketable securities.

Certain premises under the lease are accounted for as operating leases. However, for Buildings A, B, and C that we are leasing, we are deemed, in substance, to be the owner of the landlord's buildings in accordance with the application of FASB authoritative guidance. As a result, we capitalized the landlord's costs of constructing these new facilities and recognized a corresponding facility lease obligation. We also recognized, as additional facility lease obligation, reimbursements from our landlord for tenant improvement costs that we incurred since, under FASB authoritative guidance, such payments that we receive from our landlord are deemed to be a financing obligation. Monthly lease payments on these facilities are allocated between the land element of the lease (which is accounted for as an operating lease) and the facility lease obligation, based on the estimated relative fair values of the land and buildings.

As of December 31, 2010, we had capitalized the landlord's costs of constructing Buildings A and B, which totaled \$58.4 million, and of constructing Building C, which totaled \$27.8 million. Reimbursements from our landlord for Buildings A and B tenant improvement costs totaled \$56.9 million and were received by us during 2010 and 2009. Reimbursements for Building C tenant improvement costs totaled \$14.2 million and were received by us during 2010. With respect to Buildings A and B, monthly lease payments commenced in August 2009, the buildings were placed in service by us in September 2009, and the imputed interest rate applicable to our facility lease obligation is approximately 11%. With respect to Building C, monthly lease payments commenced in January 2011, the building was placed in service by us in February 2011, and the imputed interest rate applicable to our facility lease obligation is approximately 9%. At December 31, 2011 and 2010, the Buildings A and B facility lease obligation balance was \$113.0 million and \$113.7 million, respectively, and the Building C facility lease obligation balance was \$47.5 million and \$46.4 million, respectively.

### *Capital Expenditures*

Our cash expenditures for property, plant, and equipment totaled \$57.2 million in 2011, \$99.7 million in 2010, and \$97.3 million in 2009. We received \$47.5 million in 2010 and \$23.6 million in 2009 from our landlord in connection with tenant improvement costs in Buildings A, B, and C in Tarrytown, as described above. In addition, in connection with the companies' antibody collaboration, Sanofi funded \$4.8 million in 2011, \$22.9 million in 2010, and \$0.5 million in 2009 of agreed-upon capital expenditures incurred by us to expand our manufacturing capacity at our Rensselaer facilities, of which \$1.7 million was receivable at December 31, 2011.

We expect to incur capital expenditures of approximately \$50 to \$70 million in 2012, primarily in connection with tenant improvements at our leased Tarrytown facilities, capital improvements at our Rensselaer, New York manufacturing facilities, and purchases of equipment. We expect to be reimbursed for a small portion of these capital expenditures for our Rensselaer facilities by Sanofi, with the remaining amount to be funded by our existing capital resources.

### *Offering of Convertible Senior Notes*

In October 2011, we issued \$400.0 million aggregate principal amount of 1.875% convertible senior notes in a private placement. The notes were offered by the initial purchaser only to qualified institutional buyers pursuant to Rule 144A under the Securities Act of 1933.

The notes will pay interest semi-annually on April 1 and October 1, beginning April 1, 2012, and will mature on October 1, 2016, unless earlier converted or repurchased. The notes will be convertible, subject to certain conditions, into cash, shares of our Common Stock, or a combination of cash and shares of Common Stock, at our option. The initial conversion rate for the notes will be 11.9021 shares of Common Stock (subject to adjustment in certain circumstances) per \$1,000 principal amount of the notes, which is equal to an initial conversion price of approximately \$84.02 per share. A holder of the notes may surrender their notes at their option any time prior to the close of business on the business day immediately preceding July 1, 2016, only under the following circumstances: (i) during any calendar quarter commencing after the calendar quarter ending on December 31, 2011 (and only during such calendar quarter), if the last reported sale price of our Common Stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day; (ii) during the five business day period after any ten consecutive trading day period (the "measurement period") in which the trading price, as defined, of the notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our Common Stock and the conversion rate on each such trading day; (iii) if we elect to issue to all or substantially all holders of our Common Stock any rights, options, or warrants (other than pursuant to a rights plan) entitling them for a period of not more than 60 calendar days after the record date for such issuance, to subscribe for or purchase shares of our Common Stock, at a price per share less than the average of the last reported sales prices of our Common Stock for the ten consecutive day period ending on, and including, the trading day immediately preceding the declaration date for such issuance; (iv) upon specified distributions to our shareholders; or (v) upon the occurrence of specified corporate transactions, such as a fundamental change (i.e., a change in control), or our Common Stock ceasing to be listed on at least one U.S. national securities exchange. On or after July 1, 2016, holders may convert their notes at the conversion rate at any time prior to the close of business on the second scheduled trading day immediately preceding the maturity date irrespective of the foregoing conditions. In the event that a fundamental change, as defined in the indenture under which the notes have been issued, occurs prior to maturity of the notes, the initial conversion rate may be increased to include additional shares upon conversion, or holders can require us to purchase from them all or a portion of their notes for 100% of the principal value plus any accrued and unpaid interest.

In connection with the offering of the convertible senior notes, we entered into convertible note hedge (call option) and warrant transactions with multiple counterparties, including an affiliate of the initial purchaser. The convertible note hedge transactions cover, subject to customary anti-dilution adjustments, the number of shares of our Common Stock that initially underlie the notes, and are intended to reduce the potential dilutive impact of the conversion feature of the notes. The convertible note hedge will terminate upon the earlier of the maturity date of the notes or the first day the notes are no longer outstanding. The warrant transactions have an initial strike price of approximately \$103.41 per share, and may be settled in cash or shares of our Common Stock, at our option. The warrants expire at various dates during 2017.

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The net proceeds from the convertible senior notes offering were \$391.1 million after deducting the initial purchaser's discount and issuance costs. In addition, the net cost of the convertible note hedge transactions, after taking into account the proceeds received by us from the warrant transactions, was \$23.7 million. We intend to use the remaining net proceeds from the issuance of the notes for general corporate purposes.

### **Funding Requirements**

We expect to continue to incur substantial funding requirements for our research and development activities (including preclinical and clinical testing). As described above, research and development expenses that we incur in connection with our ZALTRAP<sup>®</sup> and antibodies collaborations are generally funded by Sanofi. In addition, as described above, we and Bayer HealthCare share agreed-upon development expenses that both companies incur in connection with our EYLEA<sup>®</sup> collaboration. After taking into account anticipated reimbursements from our collaborators, we currently estimate that approximately 40-50% of our funding requirements for 2012 will be directed toward technology development, basic research and early preclinical activities, and the preclinical and clinical development of our product candidates. For 2012, we also currently estimate that approximately 20-25% of our funding requirements will be directed toward the planned commercialization of new indications for our marketed products and ZALTRAP<sup>®</sup>; approximately 15-20% of our funding requirements will be applied to capital expenditures (as described above); and the remainder of our funding requirements will be used for general corporate purposes.

In connection with our funding requirements, the following table summarizes our contractual obligations as of December 31, 2011. These obligations and commitments assume non-termination of agreements and represent expected payments based on current operating forecasts, which are subject to change:

(In millions)	Total	Payments Due by Period				Greater than 5 years
		Less than one year	1 to 3 years	3 to 5 years	5 years	
Convertible senior notes (1)	\$ 437.0	\$ 7.1	\$ 15.0	\$ 414.9		
Operating leases (2)	97.2	7.3	15.0	15.3	\$ 59.6	
Capital leases	2.5	1.2	1.3			
Purchase obligations (3)	148.0	91.7	49.3	7.0		
Other long-term liabilities (4)	240.7	15.7	35.3	36.8		152.9
<b>Total contractual obligations</b>	<b>\$ 925.4</b>	<b>\$ 123.0</b>	<b>\$ 115.9</b>	<b>\$ 474.0</b>		<b>\$ 212.5</b>

- (1) Consists of \$400.0 million aggregate principal amount of 1.875% convertible senior notes that mature on October 1, 2016, unless earlier converted or repurchased. The amounts in the table above assume the payment of interest on our convertible senior notes through their maturity date and the payment of the principal amount of the notes at their maturity date. Interest on the notes is payable semi-annually. The convertible senior notes will be convertible, subject to certain conditions, into cash, shares of our Common Stock, or a combination of cash and shares of Common Stock, at our option.
- (2) Excludes future contingent costs for utilities, real estate taxes, and operating expenses. In 2011, these costs were \$9.3 million. See Note 12(a) to our Financial Statements.
- (3) Purchase obligations primarily relate to (i) research and development commitments, including those related to clinical trials, (ii) capital expenditures for equipment acquisitions, and (iii) license payments. Our obligation to pay certain of these amounts may increase or be reduced based on certain future events. Open purchase orders for the acquisition of goods and services in the ordinary course of business are excluded from the table above.
- (4) Represents payments with respect to facility lease obligations in connection with our lease of facilities in Tarrytown, New York, as described above. See Note 12(a) to our Financial Statements.

Under our collaboration with Bayer HealthCare, over the next several years we and Bayer HealthCare will share agreed-upon EYLEA<sup>®</sup> development expenses incurred by both companies, under a global development plan, as described above. In addition, under our collaboration agreements with Sanofi and Bayer HealthCare, if the applicable collaboration becomes profitable, we have contingent contractual obligations to reimburse Sanofi and Bayer HealthCare for a defined percentage (generally 50%) of agreed-upon development expenses incurred by Sanofi and Bayer HealthCare, respectively. Profitability under each collaboration will be measured by calculating net sales less agreed-upon expenses. These reimbursements would be deducted from our share of the collaboration profits (and, for our ZALTRAP<sup>®</sup> collaboration with Sanofi, royalties on product sales in Japan) otherwise payable to us, unless, in some cases, we elect to reimburse these expenses at a faster rate. Given the uncertainties related to drug development (including the development of ZALTRAP<sup>®</sup> and co-developed antibody candidates in collaboration with Sanofi and EYLEA<sup>®</sup> in collaboration with Bayer HealthCare), such as the variability in the length of time necessary to develop a product candidate and the ultimate ability to obtain governmental approval for commercialization, we are currently unable to reliably estimate if our

collaborations with Sanofi and Bayer HealthCare will become profitable.

The amount we need to fund operations will depend on various factors, including revenues from net product sales, the potential regulatory approval and commercialization of our product candidates and new indications for our marketed products, and the timing thereof, the status of competitive products, the success of our research and development programs, the potential future need to expand our professional and support staff and facilities, the status of patents and other intellectual property rights (and pending or future litigation related thereto), the delay or failure of a clinical trial of any of our potential drug candidates, and the continuation, extent, and success of our collaborations with Sanofi and Bayer HealthCare. Clinical trial costs are dependent, among other things, on the size and duration of trials, fees charged for services provided by clinical trial investigators and other third parties, the costs for manufacturing the product candidate for use in the trials, and for supplies, laboratory tests, and other expenses. The amount of funding that will be required for our clinical programs depends upon the results of our research and preclinical programs and early-stage clinical trials, regulatory requirements, the duration and results of clinical trials underway and of additional clinical trials that we decide to initiate, and the various factors that affect the cost of each trial as described above. Our commercialization costs over approximately the next few years will depend on, among other things, whether or not new indications for our marketed products or our late-stage product candidates receive regulatory approval, the market potential for such new indications or product candidates, and the commercialization terms of our collaboration agreements, if applicable (whereby some or all commercialization costs may be shared with our collaborators). Currently, we are required to pay royalties on product sales of EYLEA® for the treatment of wet AMD and ARCALYST® for the treatment of CAPS. In the future, if we are able to successfully develop, market, and sell EYLEA® or ARCALYST® for other indications, or certain of our product candidates, we may be required to pay royalties or share the profits from such sales pursuant to our license or collaboration agreements.

We expect that expenses related to the filing, prosecution, defense, and enforcement of patents and other intellectual property will continue to be substantial.

We believe that our existing capital resources, together with funds generated by anticipated EYLEA® net product sales and funding we are entitled to receive under our collaboration agreements, will enable us to meet our projected operating needs. However, this is a forward-looking statement based on our current operating plan, and there may be a change in projected revenues or expenses that would lead to our capital being consumed significantly before such time. For example, in connection with preparing to commercialize and launch potential products that are not licensed to a third party, we could incur substantial pre-marketing and commercialization expenses that could lead us to consume our cash at a faster rate. If there is insufficient capital to fund all of our planned operations and activities, we anticipate that we would (i) seek sources of additional capital through collaborative arrangements and/or additional public or private financing, including debt and equity financing and/or (ii) prioritize available capital to fund selected preclinical and clinical development programs and/or preparations for the potential commercialization of our late-stage product candidates, or license selected products.

Other than letters of credits totaling \$4.2 million, including the \$3.4 million letter of credit issued in connection with our lease for facilities in Tarrytown, New York, as described above, we have no off-balance sheet arrangements. In addition, we do not guarantee the obligations of any other entity. As of December 31, 2011, we had no other established banking arrangements through which we could obtain short-term financing or a line of credit. In October 2011, we completed a private placement of convertible senior notes, as described above. In addition, in October 2010, we filed a shelf registration statement on Form S-3 registering the sale, in one or more offerings, of an indeterminate amount of equity or debt securities, together or separately, and our October 2010 public offering of approximately 6.3 million shares of Common Stock was completed under this shelf registration statement. There is no assurance, however, that we will be able to complete any additional offerings of securities. Factors influencing the availability of additional financing include our progress in product development and commercialization, investor perception of our prospects, and the general condition of the financial markets. We may not be able to secure additional funding through new collaborative arrangements or additional public or private offerings. If we cannot raise adequate funds to satisfy our capital requirements, we may have to delay, scale-back, or eliminate certain of our research and development activities or future operations. This could materially harm our business.

## **Future Impact of Recently Issued Accounting Standards**

### *Fees paid to the federal government by pharmaceutical manufacturers*

In December 2010, the FASB provided authoritative guidance on how pharmaceutical manufacturers should recognize and classify in their income statement annual fees mandated by the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act. This guidance became effective for calendar years beginning after December 31, 2010. The adoption of this guidance did not have an impact on our financial statements for the year ended December 31, 2011, and we do not anticipate that this guidance will have a material impact on our financial statements for the year ended December 31, 2012, since (i) ARCALYST<sup>®</sup> for the treatment of CAPS, has been approved as an orphan drug and orphan drugs are not subject to this annual fee and (ii) EYLEA<sup>®</sup> received regulatory approval from the FDA, and was launched, in November 2011.

### *Presentation of comprehensive income*

In June 2011, the FASB amended its authoritative guidance on the presentation of comprehensive income. Under the amendment, an entity will have the option to present the total of comprehensive income, the components of net income, and the components of other comprehensive income either in a single continuous statement of comprehensive income or in two separate but consecutive statements. This amendment, therefore, eliminates the currently available option to present the components of other comprehensive income as part of the statement of changes in stockholders' equity. The amendment does not change the items that must be reported in other comprehensive income or when an item of other comprehensive income must be reclassified to net income. We will adopt this amended guidance for the fiscal year beginning January 1, 2012. As this guidance relates to presentation only, the adoption of this guidance will not have any other effect on our financial statements.

## **Item 7A. Quantitative and Qualitative Disclosures About Market Risk**

### *Interest Rate Risk*

Our earnings and cash flows are subject to fluctuations due to changes in interest rates, principally in connection with our investments in marketable securities, which consist primarily of direct obligations of the U.S. government and its agencies, other debt securities guaranteed by the U.S. government, and money market funds that invest in U.S. government securities. We do not believe we are materially exposed to changes in interest rates. Under our current policies, we do not use interest rate derivative instruments to manage exposure to interest rate changes. We estimate that a one percent unfavorable change in interest rates would have resulted in approximately a \$1.4 million and \$5.9 million decrease in the fair value of our unrestricted investment portfolio at December 31, 2011 and 2010, respectively. The decrease in interest rate risk year over year is due primarily to lower balances of marketable debt securities with maturities in excess of one year that we held at December 31, 2011 compared to 2010.

### *Credit Quality Risk*

We have an investment policy that includes guidelines on acceptable investment securities, minimum credit quality, maturity parameters, and concentration and diversification. Nonetheless, deterioration of the credit quality of an investment security subsequent to purchase may subject us to the risk of not being able to recover the full principal value of the security. We have recognized other-than-temporary impairment charges related to certain marketable securities of \$0.1 million in 2010 and 2009. During 2011, we did not recognize any other-than-temporary impairment charges.

We are also subject to credit risk in connection with accounts receivable from our product sales of EYLEA<sup>®</sup> and ARCALYST<sup>®</sup>. Our marketed products are sold in the United States, and related accounts receivable are due from three distributors and several specialty pharmacies, who are our customers. We have contractual payment terms with each of our customers. We monitor our customers' financial performance and credit worthiness so that we can properly assess and respond to any changes in their credit profile. During 2011, 2010, and 2009 we did not recognize any charges for write-offs of accounts receivable related to our marketed products.

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

The financial statements required by this Item are included on pages F-1 through F-38 of this report. The supplementary financial information required by this Item is included at page F-38 of this report.

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

Not applicable.

**Item 9A. Controls and Procedures**

*Evaluation of Disclosure Controls and Procedures*

The Company's management, with the participation of our chief executive officer and chief financial officer, conducted an evaluation of the effectiveness of the Company's disclosure controls and procedures (as such term is defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934 (the "Exchange Act")) as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our chief executive officer and chief financial officer each concluded that, as of the end of such period, our disclosure controls and procedures were effective in ensuring that information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized, and reported on a timely basis, and is accumulated and communicated to the Company's management, including the Company's chief executive officer and chief financial officer, as appropriate to allow timely decisions regarding required disclosure.

*Management Report on Internal Control over Financial Reporting*

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our management conducted an evaluation of the effectiveness of our internal control over financial reporting using the framework in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on that evaluation, our management has concluded that our internal control over financial reporting was effective as of December 31, 2011. The effectiveness of our internal control over financial reporting as of December 31, 2011 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report which appears herein.

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

*Changes in Internal Control over Financial Reporting*

There has been no change in our internal control over financial reporting (as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) during the quarter ended December 31, 2011 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.



Our management, including our chief executive officer and chief financial officer, does not expect that our disclosure controls and procedures or internal controls over financial reporting will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the system are met and cannot detect all deviations. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud or deviations, if any, within the company have been detected. Projections of any evaluation of effectiveness to future periods are subject to the risks that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

**Item 9B. Other Information**

None.

### **PART III**

#### **Item 10. Directors, Executive Officers and Corporate Governance**

The information required by this item (other than the information set forth in the next paragraph in this Item 10) will be included in our definitive proxy statement with respect to our 2012 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

We have adopted a code of business conduct and ethics that applies to our officers, directors, and employees. The full text of our code of business conduct and ethics can be found on our website (<http://www.regeneron.com>) under the Investors heading on the Corporate Governance page. We may satisfy the disclosure requirements under Item 5.05 of Form 8-K regarding an amendment to, or a waiver from, a provision of our code of business conduct and ethics that applies to our principal executive officer, principal financial officer, principal accounting officer, or controller, or persons performing similar functions, by posting such information on our website where it is accessible through the same link noted above.

#### **Item 11. Executive Compensation**

The information called for by this item will be included in our definitive proxy statement with respect to our 2012 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

#### **Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters**

The information called for by this item will be included in our definitive proxy statement with respect to our 2012 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

#### **Item 13. Certain Relationships and Related Transactions, and Director Independence**

The information required by this item will be included in our definitive proxy statement with respect to our 2012 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

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

The information called for by this item will be included in our definitive proxy statement with respect to our 2012 Annual Meeting of Shareholders to be filed with the SEC, and is incorporated herein by reference.

### **PART IV**

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

##### *(a) 1. Financial Statements*

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

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### 2. Financial Statement Schedules

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

### 3. Exhibits

Exhibit Number	Description	-	Description
3.1	(m)	-	Restated Certificate of Incorporation.
3.2	(a)	-	By-Laws, as amended.
4.1	(z)	-	Indenture, dated as of October 21, 2011, between Regeneron Pharmaceuticals, Inc. and Wells Fargo Bank, National Association, as Trustee.
4.2	(z)	-	Form of 1.875% Convertible Senior Note due October 1, 2016.
10.1+	(y)	-	The Second Amended and Restated 2000 Long-Term Incentive Plan.
10.1.1+	(b)	-	Form of option agreement and related notice of grant for use in connection with the grant of options to the Registrant's non-employee directors and named executive officers.
10.1.2+	(b)	-	Form of option agreement and related notice of grant for use in connection with the grant of options to the Registrant's executive officers other than the named executive officers.
10.1.3+	(c)	-	Form of restricted stock award agreement and related notice of grant for use in connection with the grant of restricted stock awards to the Registrant's executive officers.
10.1.4+	(c)	-	Form of option agreement and related notice of grant for use in connection with the grant of stock options to certain of the Registrant's executive officers in connection with a January 2005 Option Exchange Program.
10.1.5+	(q)	-	Form of option agreement and related notice of grant for use in connection with the grant of time based vesting stock options to the Registrant's non-employee directors and executive officers.
10.1.6+	(q)	-	Form of option agreement and related notice of grant for use in connection with the grant of performance based vesting stock options to the Registrant's executive officers.
10.1.7+	(x)	-	Form of restricted stock award agreement and related notice of grant for use in connection with the grant of restricted stock awards to the Registrant's executive officers (revised).
10.1.8+	(x)	-	Form of option agreement and related notice of grant for use in connection with the grant of performance based vesting stock options to the Registrant's executive officers (revised).
10.1.9+		-	Form of option agreement and related notice of grant for use in connection with the grant of time based vesting stock options to the Registrant's non-employee directors (revised).
10.2+	(p)	-	Amended and Restated Employment Agreement, dated as of November 14, 2008, between the Registrant and Leonard S. Schleifer, M.D., Ph.D.
10.3*+	(d)	-	Employment Agreement, dated as of December 31, 1998, between the Registrant and P. Roy Vagelos, M.D.
10.4+	(p)	-	Regeneron Pharmaceuticals, Inc. Change in Control Severance Plan, amended and restated effective as of November 14, 2008.
10.5*	(e)	-	IL-1 License Agreement, dated June 26, 2002, by and among the Registrant, Immunex Corporation, and Amgen Inc.
10.6*	(r)	-	IL-1 Antibody Termination Agreement by and between Novartis Pharma AG, Novartis Pharmaceuticals Corporation and the Registrant, dated as of June 8, 2009.
10.7*	(r)	-	Trap-2 Termination Agreement by and between Novartis Pharma AG, Novartis Pharmaceuticals Corporation and the Registrant, dated as of June 8, 2009.

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10.8*	(f)	-	Collaboration Agreement, dated as of September 5, 2003, by and between Aventis Pharmaceuticals Inc. and the Registrant.
10.8.1*	(d)	-	Amendment No. 1 to Collaboration Agreement, by and between Aventis Pharmaceuticals Inc. and the Registrant, effective as of December 31, 2004
10.8.2	(g)	-	Amendment No. 2 to Collaboration Agreement, by and between Aventis Pharmaceuticals Inc. and the Registrant, effective as of January 7, 2005.

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10.8.3*	(h)	-	Amendment No. 3 to Collaboration Agreement, by and between Aventis Pharmaceuticals Inc. and the Registrant, effective as of December 21, 2005.
10.8.4*	(h)	-	Amendment No. 4 to Collaboration Agreement, by and between sanofi-aventis U.S., LLC (successor in interest to Aventis Pharmaceuticals, Inc.) and the Registrant, effective as of January 31, 2006.
10.9*	(i)	-	License and Collaboration Agreement, dated as of October 18, 2006, by and between Bayer HealthCare LLC and the Registrant.
10.10	(k)	-	Lease, dated as of December 21, 2006, by and between BMR-Landmark at Eastview LLC and the Registrant.
10.10.1*	(l)	-	First Amendment to Lease, by and between BMR-Landmark at Eastview LLC and the Registrant, effective as of October 24, 2007.
10.10.2	(o)	-	Second Amendment to Lease, by and between BMR-Landmark at Eastview LLC and the Registrant, effective as of September 30, 2008.
10.10.3	(q)	-	Third Amendment to lease, by and between BMR-Landmark at Eastview LLC and the Registrant, entered into as of April 29, 2009.
10.10.4	(s)	-	Fourth Amendment to Lease, by and between BMR-Landmark at Eastview LLC and the Registrant, effective as of December 3, 2009.
10.10.5	(t)	-	Fifth Amendment to Lease, by and between BMR-Landmark at Eastview LLC and the Registrant, entered into as of February 11, 2010.
10.10.6	(v)	-	Sixth Amendment to Lease, by and between BMR-Landmark at Eastview LLC and the Registrant, entered into as of June 4, 2010.
10.10.7	(x)	-	Seventh Amendment to Lease, by and between BMR-Landmark at Eastview LLC and the Registrant, entered into as of December 22, 2010.
10.10.8	(aa)	-	Eighth Amendment to Lease, by and between BMR-Landmark at Eastview LLC and the Registrant, entered into as of August 1, 2011.
10.10.9	(aa)	-	Ninth Amendment to Lease, by and between BMR-Landmark at Eastview LLC and the Registrant, entered into as of September 30, 2011.
10.11*	(k)	-	Non Exclusive License and Material Transfer Agreement, dated as of March 30, 2007, by and between Astellas Pharma Inc. and the Registrant.
10.11.1*	(w)	-	Amendment to the Non Exclusive License and Material Transfer Agreement, dated as of March 30, 2007 by and between Astellas Pharma Inc. and the Registrant, dated as of July 28, 2010.
10.12*	(u)	-	Amended and Restated Discovery and Preclinical Development Agreement, dated as of November 10, 2009, by and between Aventis Pharmaceuticals Inc. and the Registrant.
10.13*	(u)	-	Amended and Restated License and Collaboration Agreement, dated as of November 10, 2009, by and among Aventis Pharmaceuticals Inc., sanofi-aventis Amerique Du Nord, and the Registrant.
10.14	(m)	-	Stock Purchase Agreement, dated as of November 28, 2007, by and among sanofi-aventis Amerique Du Nord, sanofi-aventis US LLC, and the Registrant.
10.15	(m)	-	Investor Agreement, dated as of December 20, 2007, by and among sanofi-aventis, sanofi-aventis US LLC, Aventis Pharmaceuticals Inc., sanofi-aventis Amerique du Nord, and the Registrant.
10.15.1	(u)	-	First Amendment to the December 20, 2007 Investor Agreement, dated as of November 10, 2009, by and among sanofi-aventis US LLC, Aventis Pharmaceuticals, Inc., sanofi-aventis Amerique du Nord, and the Registrant.
10.16*	(n)	-	Amended and Restated Non-Exclusive License Agreement, dated as of July 1, 2008 by and between Collectis, S.A. and the Registrant.
10.17	(z)	-	Purchase Agreement, dated as of October 18, 2011, between Regeneron Pharmaceuticals, Inc. and Goldman, Sachs & Co.
10.18	(z)	-	Master Terms and Conditions for Convertible Note Hedging Transactions, dated October 18, 2011, between Goldman, Sachs & Co. and Regeneron Pharmaceuticals, Inc.
10.19	(z)	-	Master Terms and Conditions for Base Warrants, dated October 18, 2011, between Goldman, Sachs & Co. and Regeneron Pharmaceuticals, Inc.
10.20	(z)	-	Master Terms and Conditions for Convertible Note Hedging Transactions, dated October 18, 2011, between Citibank, N.A. and Regeneron Pharmaceuticals, Inc.
10.21	(z)	-	Master Terms and Conditions for Base Warrants, dated October 18, 2011, between Citibank, N.A. and Regeneron Pharmaceuticals, Inc.
10.22	(z)	-	Master Terms and Conditions for Convertible Note Hedging Transactions, dated October 18, 2011, between Credit Suisse International and Regeneron Pharmaceuticals, Inc.
10.23	(z)	-	Master Terms and Conditions for Base Warrants, dated October 18, 2011, between Credit Suisse International and Regeneron Pharmaceuticals, Inc.
10.24	(z)	-	Master Terms and Conditions for Convertible Note Hedging Transactions, dated October 18, 2011, between Morgan Stanley & Co. International plc and Regeneron Pharmaceuticals, Inc.
10.25	(z)	-	Master Terms and Conditions for Base Warrants, dated October 18, 2011, between Morgan Stanley & Co. International plc and Regeneron Pharmaceuticals, Inc.
10.26**		-	Non-exclusive License and Partial Settlement Agreement with Genentech, Inc.

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23.1	-	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm.
24.1	-	Power of Attorney (included on the signature page of this Annual Report on Form 10-K).
31.1	-	Certification of CEO pursuant to Rule 13a-14(a) under the Securities Exchange Act of 1934.
31.2	-	Certification of CFO pursuant to Rule 13a-14(a) under the Securities Exchange Act of 1934.
32	-	Certification of CEO and CFO pursuant to 18 U.S.C. Section 1350.
101	-	Interactive Data File

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101.INS	-	XBRL Instance Document
101.SCH	-	XBRL Taxonomy Extension Schema
101.CAL	-	XBRL Taxonomy Extension Calculation Linkbase
101.LAB	-	XBRL Taxonomy Extension Label Linkbase
101.PRE	-	XBRL Taxonomy Extension Presentation Linkbase
101.DEF	-	XBRL Taxonomy Extension Definition Document

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- (a) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc., filed November 13, 2007.
- (b) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc., filed December 16, 2005.
- (c) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc., filed December 13, 2004.
- (d) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc., for the year ended December 31, 2004, filed March 11, 2005.
- (e) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended June 30, 2002, filed August 13, 2002.
- (f) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended September 30, 2003, filed November 12, 2003.
- (g) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc., filed January 11, 2005.
- (h) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc., for the year ended December 31, 2005, filed February 28, 2006.
- (i) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended September 30, 2006, filed November 6, 2006.
- (j) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc., for the year ended December 31, 2006, filed March 12, 2007.
- (k) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended March 31, 2007, filed May 4, 2007.
- (l) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended September 30, 2007, filed November 7, 2007.
- (m) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc., for the year ended December 31, 2007, filed February 27, 2008.
- (n) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended June 30, 2008, filed August 1, 2008.

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- (o) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended September 30, 2008, filed November 5, 2008.
- (p) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc., for the year ended December 31, 2008, filed February 26, 2009.
- (q) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended March 31, 2009, filed April 30, 2009.
- (r) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended June 30, 2009, filed August 4, 2009.
- (s) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc., filed December 8, 2009.
- (t) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc., filed February 16, 2010.
- (u) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc., for the year ended December 31, 2009, filed February 18, 2010.
- (v) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended June 30, 2010, filed July 28, 2010.
- (w) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended September 30, 2010, filed October 28, 2010.
- (x) Incorporated by reference from the Form 10-K for Regeneron Pharmaceuticals, Inc., for the year ended December 31, 2010, filed February 17, 2011.
- (y) Incorporated by reference from the Registration Statement on Form S-8 for Regeneron Pharmaceuticals, Inc., filed June 13, 2011.
- (z) Incorporated by reference from the Form 8-K for Regeneron Pharmaceuticals, Inc., filed October 24, 2011.
- (aa) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended September 30, 2011, filed October 27, 2011.

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

\*\* The Company has requested confidential treatment of certain information contained in this exhibit. Such information has been filed separately with the Commission pursuant to the Company's application for confidential treatment.

+ Indicates a management contract or compensatory plan or arrangement.



**SIGNATURES**

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

REGENERON PHARMACEUTICALS, INC.

By: /s/ LEONARD S. SCHLEIFER  
 Leonard S. Schleifer, M.D., Ph.D.  
 President and Chief Executive Officer

Dated: Tarrytown, New York  
 February 21, 2012

**POWER OF ATTORNEY**

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

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

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



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<i>/s/</i> Charles A. Baker Charles A. Baker	Director
<i>/s/</i> Michael S. Brown Michael S. Brown, M.D.	Director
<i>/s/</i> Alfred G. Gilman Alfred G. Gilman, M.D., Ph.D.	Director
<i>/s/</i> Joseph L. Goldstein Joseph L. Goldstein, M.D.	Director
<i>/s/</i> Christine A. Poon Christine A. Poon	Director
<i>/s/</i> Arthur F. Ryan Arthur F. Ryan	Director
<i>/s/</i> Eric M. Shooter Eric M. Shooter, Ph.D.	Director
<i>/s/</i> George L. Sing George L. Sing	Director
<i>/s/</i> Marc Tessier-Lavigne Marc Tessier-Lavigne, Ph.D.	Director

**REGENERON PHARMACEUTICALS, INC.**

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**REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

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

In our opinion, the accompanying balance sheets and the related statements of operations, stockholders' equity and cash flows present fairly, in all material respects, the financial position of Regeneron Pharmaceuticals, Inc., (the Company), at December 31, 2011 and December 31, 2010, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2011 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2011, based on criteria established in *Internal Control - Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company's management is responsible for these financial statements, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in Management's Report on Internal Control over Financial Reporting appearing under Item 9A. Our responsibility is to express opinions on these financial statements and on the Company's internal control over financial reporting based on our integrated audits. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits provide a reasonable basis for our opinions.

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

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

/s/ PricewaterhouseCoopers LLP

New York, New York  
February 21, 2012

**REGENERON PHARMACEUTICALS, INC.**  
**BALANCE SHEETS**  
**December 31, 2011 and 2010**  
*(In thousands, except share data)*

	2011	2010
<b>ASSETS</b>		
<b>Current assets</b>		
Cash and cash equivalents	\$ 483,610	\$ 112,572
Marketable securities	43,332	136,796
Accounts receivable from Sanofi	74,781	79,603
Accounts receivable - trade, net	28,254	2,314
Prepaid expenses and other current assets	22,898	26,337
<b>Total current assets</b>	<b>652,875</b>	<b>357,622</b>
Restricted cash and marketable securities	7,721	7,518
Marketable securities	275,887	370,053
Property, plant, and equipment, at cost, net of accumulated depreciation and amortization	367,955	347,450
Other assets	19,145	6,789
<b>Total assets</b>	<b>\$ 1,323,583</b>	<b>\$ 1,089,432</b>
<b>LIABILITIES and STOCKHOLDERS' EQUITY</b>		
<b>Current liabilities</b>		
Accounts payable and accrued expenses	\$ 95,625	\$ 53,658
Deferred revenue from Sanofi, current portion	20,011	19,506
Deferred revenue - other, current portion	31,629	35,217
Facility lease obligations, current portion	1,006	675
<b>Total current liabilities</b>	<b>148,271</b>	<b>109,056</b>
Deferred revenue from Sanofi	86,017	97,081
Deferred revenue - other	162,593	188,775
Facility lease obligations	159,508	159,355
Convertible senior notes	275,019	
Other long term liabilities	6,443	7,350
<b>Total liabilities</b>	<b>837,851</b>	<b>561,617</b>
<b>Commitments and contingencies (Note 12)</b>		
<b>Stockholders' equity</b>		
Preferred stock, \$.01 par value; 30,000,000 shares authorized; issued and outstanding - none		
Class A Stock, convertible, \$.001 par value: 40,000,000 shares authorized; shares issued and outstanding - 2,109,512 in 2011 and 2,182,036 in 2010	2	2
Common Stock, \$.001 par value; 160,000,000 shares authorized; shares issued and outstanding - 90,692,071 in 2011 and 87,238,301 in 2010	91	87
Additional paid-in capital	1,754,824	1,575,780
Accumulated deficit	(1,267,323)	(1,045,563)
Accumulated other comprehensive loss	(1,862)	(2,491)
<b>Total stockholders' equity</b>	<b>485,732</b>	<b>527,815</b>
<b>Total liabilities and stockholders' equity</b>	<b>\$ 1,323,583</b>	<b>\$ 1,089,432</b>

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

**REGENERON PHARMACEUTICALS, INC.**  
**STATEMENTS OF OPERATIONS**  
**For the Years Ended December 31, 2011, 2010, and 2009**  
*(In thousands, except per share data)*

	2011	2010	2009
<b>Revenues</b>			
Sanofi collaboration revenue	\$ 326,609	\$ 311,332	\$ 247,140
Other collaboration revenue	43,072	75,393	67,317
Net product sales	44,686	25,254	18,364
Technology licensing	24,858	40,150	40,013
Contract research and other	6,599	6,945	6,434
	445,824	459,074	379,268
<b>Expenses</b>			
Research and development	529,506	489,252	398,762
Selling, general, and administrative	117,261	65,201	52,923
Cost of goods sold	4,216	2,093	1,686
	650,983	556,546	453,371
<b>Loss from operations</b>	(205,159)	(97,472)	(74,103)
<b>Other income (expense)</b>			
Investment income	3,549	2,122	4,488
Interest expense	(21,282)	(9,118)	(2,337)
	(17,733)	(6,996)	2,151
<b>Net loss before income tax benefit</b>	(222,892)	(104,468)	(71,952)
<b>Income tax benefit</b>	(1,132)		(4,122)
<b>Net loss</b>	\$ (221,760)	\$ (104,468)	\$ (67,830)
<b>Net loss per share, basic and diluted</b>	\$ (2.45)	\$ (1.26)	\$ (0.85)
<b>Weighted average shares outstanding, basic and diluted</b>	90,610	82,926	79,782

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

**REGENERON PHARMACEUTICALS, INC.**  
**STATEMENTS OF STOCKHOLDERS' EQUITY**  
**For the Years Ended December 31, 2011, 2010, and 2009**  
*(In thousands)*

	Class A Stock		Common Stock		Additional	Accumulated	Acc
	Shares	Amount	Shares	Amount	Paid-in	Deficit	Oth
					Capital		Con
							Inco
<b>Balance, December 31, 2008</b>	2,249	\$ 2	77,642	\$ 78	\$ 1,294,813	\$ (873,265)	\$
Issuance of Common Stock in connection with exercise of stock options, net of shares tendered			1,134	1	9,269		
Issuance of Common Stock in connection with Company 401(k) Savings Plan contribution			81		1,391		
Conversion of Class A Stock to Common Stock	(4)		4				
Stock-based compensation charges					31,259		
Net loss, 2009						(67,830)	
Change in net unrealized gain (loss) on marketable securities, net of tax effect of \$0.7 million							
<b>Balance, December 31, 2009</b>	2,245	2	78,861	79	1,336,732	(941,095)	
Issuance of Common Stock in a public offering, net of issuance costs			6,325	6	174,822		
Issuance of Common Stock in connection with exercise of stock options, net of shares tendered			1,533	2	21,462		
Issuance of Common Stock in connection with Company 401(k) Savings Plan contribution			111		2,867		
Issuance of restricted Common Stock under Long-Term Incentive Plan			345				
Conversion of Class A Stock to Common Stock	(63)		63				
Stock-based compensation charges					39,897		
Net loss, 2010						(104,468)	
Change in net unrealized gain (loss) on marketable securities							
<b>Balance, December 31, 2010</b>	2,182	2	87,238	87	1,575,780	(1,045,563)	
Issuance of Common Stock in connection with exercise of stock options, net of shares tendered			3,324	4	21,171		
Issuance of Common Stock in connection with Company 401(k) Savings Plan contribution			92		6,979		
Issuance of restricted Common Stock under Long-Term Incentive Plan			16				
Restricted Common Stock tendered upon vesting in connection with employee tax obligations			(51)		(2,638)		
Conversion of Class A Stock to Common Stock	(73)		73				
Stock-based compensation charges					56,609		
Equity component of convertible senior notes, net of issuance costs					120,623		
Purchase of convertible note hedges					(117,500)		
Issuance of warrants in connection with issuance of convertible senior notes					93,800		
Net loss, 2011						(221,760)	
Change in net unrealized gain (loss) on marketable securities, net of tax effect of \$0.4 million							
<b>Balance, December 31, 2011</b>	2,109	\$ 2	90,692	\$ 91	\$ 1,754,824	\$ (1,267,323)	\$

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





**REGENERON PHARMACEUTICALS, INC.**  
**STATEMENTS OF CASH FLOWS**  
**For the Years Ended December 31, 2011, 2010, and 2009**  
*(In thousands)*

	2011	2010	2009
<b>Cash flows from operating activities</b>			
Net loss	\$ (221,760)	\$ (104,468)	\$ (67,830)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities			
Depreciation and amortization	31,082	19,687	14,247
Non-cash compensation expense	56,094	39,897	31,259
Other non-cash charges and expenses, net	10,366	3,171	2,238
Changes in assets and liabilities			
Increase in Sanofi and trade accounts receivable	(21,118)	(17,518)	(30,494)
Increase in prepaid expenses and other assets	(6,033)	(7,303)	(4,436)
(Decrease) increase in deferred revenue	(40,329)	158,151	(27,497)
Increase in accounts payable, accrued expenses, and other liabilities	50,016	7,605	12,577
Total adjustments	80,078	203,690	(2,106)
Net cash (used in) provided by operating activities	(141,682)	99,222	(69,936)
<b>Cash flows from investing activities</b>			
Purchases of marketable securities	(240,391)	(605,124)	(199,997)
Sales or maturities of marketable securities	426,356	273,723	295,117
(Increase) decrease in restricted cash and marketable securities	(277)	(5,941)	50
Capital expenditures	(57,217)	(99,689)	(97,318)
Net cash provided by (used in) investing activities	128,471	(437,031)	(2,148)
<b>Cash flows from financing activities</b>			
Proceeds in connection with facility lease obligation		47,544	23,640
Payments in connection with facility lease obligation	(674)	(924)	(875)
Payments in connection with capital lease obligation	(993)	(104)	
Proceeds in connection with issuance of convertible notes, net of debt issuance costs	391,107		
Proceeds in connection with issuance of warrants	93,800		
Payment in connection with purchase of convertible note hedges	(117,500)		
Net proceeds in connection with issuances of Common Stock	18,509	196,790	8,598
Net cash provided by financing activities	384,249	243,306	31,363
<b>Net increase (decrease) in cash and cash equivalents</b>	<b>371,038</b>	<b>(94,503)</b>	<b>(40,721)</b>
Cash and cash equivalents at beginning of period	112,572	207,075	247,796
Cash and cash equivalents at end of period	\$ 483,610	\$ 112,572	\$ 207,075
<b>Supplemental disclosure of cash flow information</b>			
Cash paid for interest	\$ 14,725	\$ 12,737	\$ 2,525

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

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS**

**For the years ended December 31, 2011, 2010, and 2009**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

**1. Organization and Business**

Regeneron Pharmaceuticals, Inc. (the Company or Regeneron) was incorporated in January 1988 in the State of New York. The Company is a fully integrated biopharmaceutical company that discovers, invents, develops, manufactures, and commercializes medicines for the treatment of serious medical conditions. In 2008, the Company received marketing approval from the U.S. Food and Drug Administration (FDA) for the Company's first commercial drug product, ARCALYST® (rilonacept) Injection for Subcutaneous Use for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS). In November 2011, the Company received marketing approval from the FDA for EYLEA® (aflibercept) Injection for the treatment of neovascular wet age-related macular degeneration (wet AMD). The Company's facilities are primarily located in New York. The Company's business is subject to certain risks including, but not limited to, uncertainties relating to conducting pharmaceutical research, obtaining regulatory approvals, commercializing products, and obtaining and enforcing patents.

**2. Summary of Significant Accounting Policies**

***Cash and Cash Equivalents***

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

***Marketable Securities***

The Company has an investment policy that includes guidelines on acceptable investment securities, minimum credit quality, maturity parameters, and concentration and diversification. The Company has invested its excess cash primarily in direct obligations of the U.S. government and its agencies, other debt securities guaranteed by the U.S. government, and money market funds that invest in U.S. government securities. The Company considers its marketable securities to be available-for-sale, as defined by authoritative guidance issued by the Financial Accounting Standards Board (FASB). These assets are carried at fair value and the unrealized gains and losses are included in accumulated other comprehensive income (loss) as a separate component of stockholders' equity. If the decline in the value of a marketable security in the Company's investment portfolio is deemed to be other-than-temporary, the Company writes down the security to its current fair value and recognizes a loss as a charge against income. As described under Use of Estimates below, the Company reviews its portfolio of marketable securities, using both quantitative and qualitative factors, to determine if declines in fair value below cost are other-than-temporary.

***Accounts Receivable - Trade***

The Company's trade accounts receivable represents amounts due from its distributors and specialty pharmacies (collectively, the Company's customers), which are all located in the United States. The Company monitors the financial performance and credit worthiness of its large customers so that it can properly assess and respond to changes in their credit profile. The Company provides reserves against trade receivables for estimated losses that may result from a customer's inability to pay. Amounts determined to be uncollectible are written-off against the reserve. As of December 31, 2011 and 2010, there were no reserves against trade accounts receivable. In addition, during the years ended December 31, 2011, 2010 and 2009, no trade accounts receivable were written-off.

***Inventory***

Inventories are stated at the lower of cost or estimated realizable value. The Company determines the cost of inventory using the first-in, first-out, or FIFO, method. The Company capitalizes inventory costs associated with the Company's products prior to regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized; otherwise, such costs are expensed as research and development. The Company periodically analyzes its inventory levels to identify inventory that may expire prior to expected sale or has a cost basis in excess of its estimated realizable value, and writes-down such inventories as appropriate. In addition, the Company's products are subject to strict quality control and monitoring which the Company performs throughout the manufacturing process. If certain batches or units of product no longer meet quality specifications or become obsolete due to expiration, the Company records a charge to cost of goods sold to write down such unmarketable inventory to its estimated realizable value.



**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

***Property, Plant, and Equipment***

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

Building and improvements	10-40 years
Laboratory and other equipment	3-10 years
Furniture and fixtures	5 years

Leasehold improvements are amortized over the shorter of the estimated useful lives of the assets or the lease term, without assuming renewal features, if any, are exercised. Costs of construction of certain long-lived assets include capitalized interest which is amortized over the estimated useful life of the related asset.

***Accounting for the Impairment of Long-Lived Assets***

The Company periodically assesses the recoverability of long-lived assets, such as property, plant, and equipment, and evaluates such assets for impairment whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Asset impairment is determined to exist if estimated future undiscounted cash flows are less than the carrying amount. For all periods presented, no impairment losses were recorded.

***Patents***

As a result of the Company's research and development efforts, the Company obtains and applies for patents to protect proprietary technology and inventions. All costs associated with patents for product candidates under development are expensed as incurred. Patent costs related to commercial products are capitalized and amortized over the shorter of their estimated useful life or the remaining patent term. To date, the Company has no capitalized patent costs.

***Operating Leases***

On certain of its operating lease agreements, the Company may receive rent holidays and other incentives. The Company recognizes operating lease costs on a straight-line basis without regard to deferred payment terms, such as rent holidays, that defer the commencement date of required payments. In addition, lease incentives that the Company receives are treated as a reduction of rent expense over the term of the related agreements.

***Revenue Recognition***

**a. Collaboration Revenue**

The Company earns collaboration revenue in connection with collaboration agreements to develop and commercialize product candidates and utilize the Company's technology platforms. The terms of these agreements typically include non-refundable up-front licensing payments, research progress (milestone) payments, and payments for development activities. Non-refundable up-front license payments, where continuing involvement is required of the Company, are deferred and recognized over the related performance period. The Company estimates its performance period based on the specific terms of each agreement, and adjusts the performance periods, if appropriate, based on the applicable facts and circumstances. Although the Company did not enter into, or materially modify, any collaboration arrangements with multiple-deliverables during the year ended December 31, 2011, any future arrangements with multiple deliverables will be divided into separate units of accounting if the deliverables in the arrangement meet certain criteria, including whether the delivered item or items has value to the collaborator on a standalone basis. Payments which are based on achieving a specific performance milestone, involving a degree of risk, are recognized as revenue when the milestone is achieved and the related payment is due and non-refundable, provided there is no future service

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obligation associated with that milestone. Substantive performance milestones typically consist of significant achievements in the development life-cycle of the related product candidate, such as completion of clinical trials, filing for approval with regulatory agencies, and receipt of approvals by regulatory agencies. In determining whether a payment is deemed to be a substantive performance milestone, the Company takes into consideration (i) the enhancement in value to the related development product candidate, (ii) the Company's performance and relative level of effort required to achieve the milestone, (iii) whether the milestone relates solely to past performance, and (iv) whether the milestone payment is considered reasonable relative to all of the deliverables and payment terms. Payments for achieving milestones which are not considered substantive are deferred and recognized over the related performance period.

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**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

The Company enters into collaboration agreements that include varying arrangements regarding which parties perform and bear the costs of research and development activities. The Company may share the costs of research and development activities with a collaborator, such as in the Company's EYLEA® collaboration with Bayer HealthCare LLC, or the Company may be reimbursed for all or a significant portion of the costs of the Company's research and development activities, such as in the Company's ZALTRAP® (pafilibercept) and antibody collaborations with Sanofi. The Company records its internal and third-party development costs associated with these collaborations as research and development expenses. When the Company is entitled to reimbursement of all or a portion of the research and development expenses that it incurs under a collaboration, the Company records those reimbursable amounts as collaboration revenue proportionately as the Company recognizes its expenses. If the collaboration is a cost-sharing arrangement in which both the Company and its collaborator perform development work and share costs, in periods when the Company's collaborator incurs development expenses that benefit the collaboration and Regeneron, the Company also recognizes, as additional research and development expense, the portion of the collaborator's development expenses that the Company is obligated to reimburse. In certain cases, the Company may also share the costs of pre-launch commercialization activities with its collaborators. The Company records its share of these costs as a reduction of collaboration revenue.

In connection with non-refundable licensing payments, the Company's performance period estimates are principally based on projections of the scope, progress, and results of its research and development activities. Due to the variability in the scope of activities and length of time necessary to develop a drug product, changes to development plans as programs progress, and uncertainty in the ultimate requirements to obtain governmental approval for commercialization, revisions to performance period estimates are likely to occur periodically, and could result in material changes to the amount of revenue recognized each year in the future. In addition, estimated performance periods may change if development programs encounter delays, or the Company and its collaborators decide to expand or contract the clinical plans for a drug candidate in various disease indications. Also, if a collaborator terminates an agreement in accordance with the terms of the agreement, the Company would recognize any unamortized remainder of an up-front or previously deferred payment at the time of the termination.

b. *VelocImmune*® Technology Licensing

The Company enters into non-exclusive license agreements with third parties that allow the third party to utilize the Company's *VelocImmune*® technology in its internal research programs. The terms of these agreements include up-front payments and entitle the Company to receive royalties on any future sales of products discovered by the third party using the Company's *VelocImmune*® technology. Up-front payments under these agreements, where continuing involvement is required of the Company, are deferred and recognized ratably over their respective license periods.

c. Product Revenue

Product sales consist of U.S. sales of the Company's two marketed products, EYLEA® and ARCALYST®. Revenue from product sales is recognized when persuasive evidence of an arrangement exists, title to product and associated risk of loss have passed to the customer, the price is fixed or determinable, collection from the customer is reasonably assured, the Company has no further performance obligations, and returns can be reasonably estimated. The Company's written contracts with its customers stipulate product is shipped freight on board destination (FOB destination). The Company records revenue from product sales upon delivery to its customers.

The Company sells EYLEA® in the United States to three distributors and several specialty pharmacies. The Company sells ARCALYST® in the United States to two specialty pharmacies. Under these distribution models, the distributors and specialty pharmacies generally take physical delivery of product. For EYLEA®, the distributors and specialty pharmacies generally sell the product directly to healthcare providers; whereas for ARCALYST®, the specialty pharmacies sell the product directly to patients.

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

Revenue from product sales are recorded net of applicable provisions for prompt pay discounts, rebates and chargebacks under governmental programs (including Medicaid), product returns, distribution-related fees, and other sales-related deductions. Calculating these provisions involves estimates and judgments. The Company reviews its estimates of rebates, chargebacks, and other applicable provisions each period and records any necessary adjustments in the current period's net product sales.

*Prompt Pay Discounts:* No prompt pay discounts are currently offered to the Company's customers on sales of EYLEA®. In connection with sales of ARCALYST®, the Company offers discounts to its customers for prompt payments. The Company estimates these discounts based on customer terms and historical experience, and expects that its customers will always take advantage of this discount. Therefore, the Company accrues 100% of the prompt pay discount that is based on the gross amount of each ARCALYST® invoice, at the time of sale.

The Company's accrual for prompt pay discounts was not material at December 31, 2011 and 2010.

*Government Rebates and Chargebacks:* The Company estimates reductions to product sales for Medicaid and Veterans Administration (VA) programs, and for certain other qualifying federal and state government programs. Based upon the Company's contracts with government agencies, statutorily-defined discounts applicable to government-funded programs, historical experience, and, in the case of EYLEA®, estimated payer mix based on third-party market research data, the Company estimates and records an allowance for rebates and chargebacks. The Company's liability for Medicaid rebates consists of estimates for claims that a state will make for a current quarter, claims for prior quarters that have been estimated for which an invoice has not been received, and invoices received for claims from prior quarters that have not been paid. The Company's reserves related to discounted pricing offered to VA, Public Health Services (PHS), and other institutions (collectively, "qualified healthcare providers") represent the Company's estimated obligations resulting from contractual commitments to sell products to qualified healthcare providers at prices lower than the list prices the Company charges to its customers (i.e., distributors and specialty pharmacies). The Company's customers charge the Company for the difference between what they pay for the products and the ultimate selling price to the qualified healthcare providers. The Company's reserve for this discounted pricing is based on expected sales to qualified healthcare providers and the chargebacks that customers have already claimed.

The Company's government rebate and chargeback accruals were \$0.6 million at December 31, 2011, which was based on a percentage of gross sales. Government rebate and chargeback accruals were not material at December 31, 2010.

*Product Returns:* Consistent with industry practice, the Company offers its customers a limited right to return product purchased directly from the Company, which is principally based upon the product's expiration date. The Company will accept returns for three months prior to and up to six months after the product expiration date. Product returned is generally not resalable given the nature of the Company's products and method of administration. The Company develops estimates for product returns based upon historical experience, inventory levels in the distribution channel, and other relevant factors.

The Company has developed estimates for EYLEA® product returns, based on several factors, including (i) the Company's historical experience to date, and the Company's expectation, that its customers will not stock significant supplies of EYLEA® due to contractual limitations and other mitigating circumstances, (ii) historical industry information regarding product return rates for similar specialty products, and (iii) the shelf life of the product. Estimates for ARCALYST® product returns have been developed based primarily on historical returns experience; to date, actual ARCALYST® product returns have been negligible. The Company monitors product supply levels in the distribution channel, as well as sales by its customers of EYLEA® to healthcare providers and ARCALYST® to patients using product-specific data provided by its customers. If necessary, the Company's estimates of product returns may be adjusted in the future based on actual returns experience, known or expected changes in the marketplace, or other factors.

The Company's product returns accruals were not material at December 31, 2011 and 2010.

*Distribution-Related Fees:* The Company has written contracts with its customers that include terms for distribution-related fees. The Company estimates and records distribution and related fees due to its customers based on a percentage of gross sales. The Company's accrual for distribution-related fees was \$1.5 million at December 31, 2011. The Company's accrual for distribution-related fees at December 31, 2010 was not material.





**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

***Investment Income***

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

***Research and Development Expenses***

Research and development expenses include costs directly attributable to the conduct of research and development programs, including the cost of salaries, payroll taxes, employee benefits, materials, supplies, depreciation on and maintenance of research equipment, costs related to research collaboration and licensing agreements, the cost of services provided by outside contractors, including services related to the Company's clinical trials, clinical trial expenses, the full cost of manufacturing drug for use in research, preclinical development, and clinical trials, amounts that the Company is obligated to reimburse to collaborators for research and development expenses that they incur, and the allocable portions of facility costs, such as rent, utilities, insurance, repairs and maintenance, depreciation, and general support services. All costs associated with research and development are expensed.

Clinical trial costs are a significant component of research and development expenses and include costs associated with third-party contractors. The Company outsources a substantial portion of its clinical trial activities, utilizing external entities such as contract research organizations (CROs), independent clinical investigators, and other third-party service providers to assist the Company with the execution of its clinical studies. For each clinical trial that the Company conducts, certain clinical trial costs are expensed immediately, while others are expensed over time based on the expected total number of patients in the trial, the rate at which patients enter the trial, and/or the period over which clinical investigators or CROs are expected to provide services.

Clinical activities which relate principally to clinical sites and other administrative functions to manage the Company's clinical trials are performed primarily by CROs. CROs typically perform most of the start-up activities for the Company's trials, including document preparation, site identification, screening and preparation, pre-study visits, training, and program management. On a budgeted basis, these start-up costs are typically 10% to 20% of the total contract value. On an actual basis, this percentage range can be significantly wider, as many of the Company's contracts with CROs are either expanded or reduced in scope compared to the original budget, while start-up costs for the particular trial may not change materially. These start-up costs usually occur within a few months after the contract has been executed and are event driven in nature. The remaining activities and related costs, such as patient monitoring and administration, generally occur ratably throughout the life of the individual contract or study. In the event of early termination of a clinical trial, the Company accrues and recognizes expenses in an amount based on its estimate of the remaining non-cancelable obligations associated with the winding down of the clinical trial and/or penalties.

For clinical study sites, where payments are made periodically on a per-patient basis to the institutions performing the clinical study, the Company accrues expense on an estimated cost-per-patient basis, based on subject enrollment and activity in each quarter. The amount of clinical study expense recognized in a quarter may vary from period to period based on the duration and progress of the study, the activities to be performed by the sites each quarter, the required level of patient enrollment, the rate at which patients actually enroll in and drop-out of the clinical study, and the number of sites involved in the study. Clinical trials that bear the greatest risk of change in estimates are typically those that have a significant number of sites, require a large number of patients, have complex patient screening requirements, and span multiple years. During the course of a trial, the Company adjusts its rate of clinical expense recognition if actual results differ from the Company's estimates. The Company's estimates and assumptions for clinical expense recognition could differ significantly from its actual results, which could cause material increases or decreases in research and development expenses in future periods when the actual results become known.

***Stock-based Compensation***

The Company recognizes stock-based compensation expense for grants of stock option awards and restricted stock under the Company's Long-Term Incentive Plan to employees and non-employee members of the Company's board of directors based on the grant-date fair value of those awards. The grant-date fair value of an award is generally recognized as compensation expense over the award's requisite service period. In addition, the Company has granted performance-based stock option awards which vest based upon the optionee satisfying certain performance and service conditions as defined in the agreements. Potential compensation cost, measured on the grant date, related to these performance options will be recognized only if, and when, the Company estimates that these options will vest, which is based on whether the Company considers the options' performance conditions to be probable of attainment. The Company's estimates of the number of performance-based options that will vest will be revised, if necessary, in subsequent periods.



**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

The Company uses the Black-Scholes model to compute the estimated fair value of stock option awards. Using this model, fair value is calculated based on assumptions with respect to (i) expected volatility of the Company's Common Stock price, (ii) the periods of time over which employees and members of the board of directors are expected to hold their options prior to exercise (expected lives), (iii) expected dividend yield on the Common Stock, and (iv) risk-free interest rates. Stock-based compensation expense also includes an estimate, which is made at the time of grant, of the number of awards that are expected to be forfeited. This estimate is revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

***Income Taxes***

The Company recognizes deferred tax liabilities and assets for the expected future tax consequences of events that have been included in the financial statements or tax returns. Under this method, deferred tax liabilities and assets are determined on the basis of the difference between the tax basis of assets and liabilities and their respective financial reporting amounts (temporary differences) at enacted tax rates in effect for the years in which the differences are expected to reverse. A valuation allowance is established for deferred tax assets for which it is more likely than not that some portion or all of the deferred tax assets will not be realized.

Uncertain tax positions are accounted for in accordance with FASB authoritative guidance, which prescribes a comprehensive model for the manner in which a company should recognize, measure, present, and disclose in its financial statements all material uncertain tax positions that the company has taken or expects to take on a tax return. Those positions, for which management's assessment is that there is more than a 50% probability of sustaining the position upon challenge by a taxing authority based upon its technical merits, are subjected to certain measurement criteria.

The Company's policy is to recognize interest and penalties related to income tax matters in income tax expense.

***Comprehensive Income (Loss)***

Comprehensive income (loss) of the Company includes net income (loss) adjusted for the change in net unrealized gain or loss on marketable securities, net of any tax effect. Comprehensive income (loss) for the years ended December 31, 2011, 2010, and 2009 have been included in the Statements of Stockholders' Equity.

***Concentration of Credit Risk***

Financial instruments which potentially subject the Company to concentrations of credit risk consist of cash, cash equivalents, marketable securities (see Note 6), and accounts receivable.

***Per Share Data***

Net income (loss) per share, basic and diluted, is computed on the basis of the net income (loss) for the period divided by the weighted average number of shares of Common Stock and Class A Stock outstanding during the period. Basic net income (loss) per share excludes restricted stock awards until vested. Diluted net income per share is based upon the weighted average number of shares of Common Stock and Class A Stock outstanding, and of common stock equivalents outstanding when dilutive. Common stock equivalents include: (i) outstanding stock options and restricted stock awards under the Company's Long-Term Incentive Plans, which are included under the treasury stock method when dilutive, (ii) Common Stock to be issued upon the assumed conversion of the Company's convertible senior notes, which are included under the if-converted method when dilutive, and (iii) Common Stock to be issued upon the exercise of outstanding warrants, which are included under the treasury stock method when dilutive. The computation of diluted net loss per share for the years ended December 31, 2011, 2010, and 2009 does not include common stock equivalents, since such inclusion would be antidilutive.

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

***Risks and Uncertainties***

Developing and commercializing new medicines entails significant risk and expense. Before revenues from the commercialization of the Company's current or future product candidates can be realized, the Company (or its 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 the Company's products and technologies uncompetitive or obsolete. The Company may be subject to legal claims by third parties seeking to enforce patents to limit or prohibit the Company from marketing or selling its products. The Company is also dependent upon the services of its employees, consultants, collaborators, and certain third-party suppliers, including single-source unaffiliated third-party suppliers of certain raw materials and equipment. Regeneron, as licensee, licenses certain technologies that are important to the Company's business which impose various obligations on the Company. If Regeneron fails to comply with these requirements, licensors may have the right to terminate the Company's licenses.

The Company has generally incurred net losses and negative cash flows from operations since its inception. The Company received regulatory approval from the FDA for ARCALYST® for the treatment of CAPS in February 2008 and EYLEA® for the treatment of wet AMD in November 2011; however, the Company has not generated significant sales or profits to date from these two drug products. Revenues to date have principally been limited to (i) up-front, license, milestone, and reimbursement payments from the Company's collaborators and other entities related to the Company's development activities and technology platforms, (ii) ARCALYST® and EYLEA® product sales, (iii) payments for past contract manufacturing activities, and (iv) investment income. Collaboration revenue in 2011 was earned from Sanofi and Bayer HealthCare under collaboration agreements (see Note 3 for the terms of these agreements). These collaboration agreements contain early termination provisions that are exercisable by Sanofi or Bayer HealthCare, as applicable.

***Use of Estimates***

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates. Estimates which could have a significant impact on the Company's financial statements include:

- Product rebates, chargebacks, and returns in connection with the recognition of product sales revenue.
- Periods over which payments, including non-refundable up-front, license, and milestone payments, are recognized as revenue in connection with collaboration and other agreements to develop and commercialize product candidates and utilize the Company's technology platforms.
- Periods over which certain clinical trial costs, including costs for clinical activities performed by contract research organizations, are recognized as research and development expenses.
- In connection with the recognition of expense, using a blended royalty rate, related to the Company's non-exclusive license with Genentech, Inc. the Company's estimate of cumulative EYLEA® sales through May 7, 2016 (see Note 12b).
- In connection with stock option awards, (i) the fair value of stock options on their date of grant using the Black-Scholes option-pricing model, based on assumptions with respect to (a) expected volatility of the Company's Common Stock price, (b) the periods of time for which employees and members of the Company's board of directors are expected to hold their options prior to exercise (expected lives), (c) expected dividend yield on the Company's Common Stock, and (d) risk-free interest rates, which are based on quoted U.S. Treasury rates for securities with maturities approximating the options' expected lives; (ii) the number of stock option awards that are expected to be forfeited; and (iii) with respect to performance-based stock option awards, if and when the options' performance conditions are considered to be probable of attainment.
- The Company's determination of whether marketable securities are other-than-temporarily impaired. The Company conducts a review of its portfolio of marketable securities, using both quantitative and qualitative factors, to determine, for securities whose current fair value is less than their cost, whether the decline in fair value below cost is other-than-temporary. In making this determination, the Company considers factors such as the length of time and the extent to which fair value has been less than cost, financial condition and near-term prospects of the issuer, recommendations of investment advisors, and forecasts of economic, market, or industry trends. This review process also includes an evaluation of the Company's ability and intent to hold individual securities until they mature or their full value can be recovered. This review is subjective and requires a high degree of judgment.

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- Useful lives of property, plant, and equipment.
- Inventory that may expire prior to expected sale or has a cost basis in excess of its estimated realizable value, which is written-down, as appropriate. In addition, capitalization of inventory costs associated with the Company's products prior to regulatory approval when, based on management's judgment, future commercialization is considered probable and the future economic benefit is expected to be realized.
- The extent to which deferred tax assets and liabilities are offset by a valuation allowance.

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**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

In addition, the Company's share of EYLEA® development expenses incurred by Bayer HealthCare, including the Company's share of Bayer HealthCare's estimated EYLEA® development expenses for the most recent fiscal quarter, are included in research and development expenses. The Bayer HealthCare estimate for the most recent fiscal quarter is adjusted in the subsequent quarter to reflect actual expenses for the quarter. Also, the Company's share of ZALTRAP® pre-launch commercialization expenses incurred by Sanofi, including the Company's share of Sanofi's estimated ZALTRAP® pre-launch commercialization expenses for the most recent fiscal quarter, are included as a reduction of Sanofi collaboration revenue. The Sanofi estimate for the most recent fiscal quarter is adjusted in the subsequent quarter to reflect actual expenses for the quarter.

***Impact of Recently Issued Accounting Standards***

**Multiple-deliverable revenue arrangements**

During the first quarter of 2011 the Company adopted amended authoritative guidance issued by the FASB on multiple-deliverable revenue arrangements. The amended guidance provides greater ability to separate and allocate consideration to be received in a multiple-deliverable revenue arrangement by requiring the use of estimated selling prices to allocate the consideration, thereby eliminating the use of the residual method of allocation. The amended guidance also requires expanded qualitative and quantitative disclosures surrounding multiple-deliverable revenue arrangements. The Company is applying this amended guidance prospectively for new or materially modified arrangements, of which there were none during the year ended December 31, 2011; therefore, the adoption of this guidance did not have an impact on the Company's financial statements.

**Milestone method of revenue recognition**

During the first quarter of 2011, the Company adopted amended authoritative guidance issued by the FASB codifying the milestone method of revenue recognition as an acceptable revenue recognition model when a milestone is deemed to be substantive. The Company earns substantive performance milestone payments in connection with its collaboration agreements to develop and commercialize product candidates with Sanofi and Bayer HealthCare. Descriptions of these collaboration agreements, including various financial terms and conditions, are provided in Note 3. Since the Company has historically accounted for milestones under the milestone method, the adoption of this guidance did not have a material impact on the Company's financial statements.

**Fees paid to the federal government by pharmaceutical manufacturers**

In December 2010, the FASB provided authoritative guidance on how pharmaceutical manufacturers should recognize and classify in their income statement annual fees mandated by the Patient Protection and Affordable Care Act as amended by the Health Care and Education Reconciliation Act. This guidance became effective for calendar years beginning after December 31, 2010. The adoption of this guidance did not have an impact on the Company's financial statements for the year ended December 31, 2011, since (i) ARCALYST® for the treatment of CAPS, has been approved as an orphan drug and orphan drugs are not subject to this annual fee and (ii) since EYLEA® received regulatory approval from the FDA, and was launched, in November 2011.

**Presentation of comprehensive income**

In June 2011, the FASB amended its authoritative guidance on the presentation of comprehensive income. Under the amendment, an entity will have the option to present the total of comprehensive income, the components of net income, and the components of other comprehensive income either in a single continuous statement of comprehensive income or in two separate but consecutive statements. This amendment, therefore, eliminates the currently available option to present the components of other comprehensive income as part of the statement of changes in stockholders' equity. The amendment does not change the items that must be reported in other comprehensive income or when an item of other comprehensive income must be reclassified to net income. The Company will adopt this amended guidance for the fiscal year beginning January 1, 2012. As this guidance relates to presentation only, the adoption of this guidance will not have any other effect on the Company's financial statements.

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

***Reclassifications***

Certain reclassifications have been made to prior period amounts to conform with the current period's presentation.

**3. Collaboration and Contract Research Agreements**

The Company has entered into various agreements related to its activities to develop and commercialize product candidates and utilize its technology platforms. Significant agreements of this kind are described below.

***a. Sanofi***

As described in Note 13, Sanofi has purchased a total of 15,816,953 shares of the Company's Common Stock, principally in connection with the companies' ZALTRAP® and antibody collaborations described below. Total Company-incurred expenses associated with these Sanofi collaborations, which include reimbursable and non-reimbursable amounts and an allocable portion of general and administrative costs, were \$318.2 million in 2011, \$282.4 million in 2010, and \$209.4 million in 2009.

***ZALTRAP® (aflibercept)***

In September 2003, the Company entered into a collaboration agreement (the ZALTRAP® Agreement) with Aventis Pharmaceuticals Inc. (predecessor to Sanofi U.S.), to jointly develop and commercialize ZALTRAP®. In connection with this agreement, Sanofi made a non-refundable up-front payment of \$80.0 million and purchased 2,799,552 newly issued unregistered shares of the Company's Common Stock for \$45.0 million.

In January 2005, the Company and Sanofi amended the ZALTRAP® Agreement to exclude intraocular delivery of aflibercept to the eye (Intraocular Delivery) from joint development under the agreement, and product rights to aflibercept in Intraocular Delivery reverted to Regeneron. In connection with this amendment, Sanofi made a \$25.0 million non-refundable payment to Regeneron (the Intraocular Termination Payment).

In December 2005, the Company and Sanofi amended the ZALTRAP® Agreement to expand the territory in which the companies are collaborating on the development of ZALTRAP® to include Japan. In connection with this amendment, Sanofi agreed to make a \$25.0 million non-refundable up-front payment to the Company, which was received in January 2006. Under the ZALTRAP® Agreement, as amended, the Company and Sanofi will share co-promotion rights and profits on sales, if any, of ZALTRAP® outside of Japan, for disease indications included in the companies' collaboration. The Company is entitled to a royalty of approximately 35% on annual sales of ZALTRAP® in Japan, subject to certain potential adjustments. The Company may also receive up to \$400 million in substantive milestone payments upon receipt of specified marketing approvals, including up to \$360 million in milestone payments related to the receipt of marketing approvals for up to eight ZALTRAP® oncology and other indications in the United States or the European Union and up to \$40 million related to the receipt of marketing approvals for up to five ZALTRAP® oncology indications in Japan.

Under the ZALTRAP® Agreement, as amended, agreed upon worldwide development expenses incurred by both companies during the term of the agreement will be funded by Sanofi. If the collaboration becomes profitable, Regeneron will be obligated to reimburse Sanofi for 50% of these development expenses, or half of \$763.4 million as of December 31, 2011, in accordance with a formula based on the amount of development expenses and Regeneron's share of the collaboration profits and Japan royalties, or at a faster rate at Regeneron's option. Regeneron has the option to conduct additional pre-Phase III studies at its own expense. In connection with the January 2005 amendment to the ZALTRAP® Agreement, the Intraocular Termination Payment of \$25.0 million will also be subject to 50% reimbursement by Regeneron to Sanofi if the collaboration becomes profitable. In addition, if the first commercial sale of an aflibercept product in Intraocular Delivery predates the first commercial sale of a ZALTRAP® product under the collaboration by two years, Regeneron will begin reimbursing Sanofi for up to \$7.5 million of ZALTRAP® development expenses in accordance with a formula until the first commercial ZALTRAP® sale under the collaboration occurs.





**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

Sanofi has the right to terminate the agreement without cause with at least twelve months advance notice. Upon termination of the agreement for any reason, Regeneron's obligation to reimburse Sanofi, for 50% of ZALTRAP® development expenses will terminate, and the Company will retain all rights to ZALTRAP®.

In accordance with the Company's revenue recognition policy described in Note 2, the up-front payments received in September 2003 and January 2006, of \$80.0 million and \$25.0 million, respectively, and reimbursement of Regeneron-incurred development expenses, are being recognized as collaboration revenue over the related performance period. In addition, in 2011, the Company and Sanofi began equally sharing ZALTRAP®-pre-launch commercialization expenses under the ZALTRAP® Agreement. The Company's share of these expenses was \$9.3 million in 2011, which reduced collaboration revenue in connection with the ZALTRAP® Agreement.

The Company recognized \$17.5 million, \$26.4 million, and \$36.5 million of collaboration revenue in 2011, 2010, and 2009, respectively, in connection with the ZALTRAP® Agreement, as amended. In connection with the ZALTRAP® Agreement, (i) at December 31, 2011, there was a net payable of \$3.7 million to Sanofi, (ii) at December 31, 2010, amounts receivable from Sanofi were \$3.9 million, and (iii) deferred revenue at December 31, 2011 and 2010 was \$22.9 million and \$32.6 million, respectively.

*Antibodies*

In November 2007, the Company entered into a global, strategic collaboration (the Antibody Collaboration) with Sanofi to discover, develop, and commercialize fully human monoclonal antibodies. In connection with the collaboration, in December 2007, Sanofi purchased 12 million newly issued, unregistered shares of the Company's Common Stock for \$312.0 million (see Note 13).

The Antibody Collaboration is governed by a Discovery and Preclinical Development Agreement (the Discovery Agreement) and a License and Collaboration Agreement (the License Agreement). In connection with the execution of the Discovery Agreement in 2007, the Company received a non-refundable up-front payment of \$85.0 million from Sanofi. In addition, under the Discovery Agreement, Sanofi is funding the Company's research to identify and validate potential drug discovery targets and develop fully human monoclonal antibodies against these targets. In November 2009, the Company and Sanofi amended these collaboration agreements to expand and extend the Antibody Collaboration. Pursuant to the Discovery Agreement, as amended, Sanofi agreed to fund up to \$160 million per year of the Company's research activities in 2010 through 2017, subject to a one-time option for Sanofi to adjust the maximum reimbursement amount down to \$120 million per year commencing in 2014 if over the prior two years certain specified criteria were not satisfied. In 2010, as the Company scaled up its capacity to conduct antibody discovery activities, Sanofi funded \$137.7 million of the Company's preclinical research under the amended Discovery Agreement. The balance between that amount and \$160 million, or \$22.3 million, has been added to the funding otherwise available to the Company in 2011-2012 under the amended Discovery Agreement. The amended Discovery Agreement will expire on December 31, 2017; however, Sanofi has an option to extend the agreement for up to an additional three years for further antibody development and preclinical activities.

For each drug candidate identified under the Discovery Agreement, Sanofi has the option to license rights to the candidate under the License Agreement. If it elects to do so, Sanofi will co-develop the drug candidate with the Company through product approval. Under certain defined circumstances, upon exercising its option to license rights to particular candidates, Sanofi must make a \$10 million substantive milestone payment to the Company. If Sanofi does not exercise its option to license rights to a particular drug candidate under the License Agreement, the Company retains the exclusive right to develop and commercialize such drug candidate, and Sanofi will receive a royalty on sales, if any. The Company and Sanofi are currently co-developing seven therapeutic antibodies under the License Agreement.

Under the License Agreement, agreed upon worldwide development expenses incurred by both companies during the term of the agreement are funded by Sanofi, except that following receipt of the first positive Phase 3 trial results for a co-developed drug candidate, subsequent Phase 3 trial-related costs for that drug candidate ( Shared Phase 3 Trial Costs ) are shared 80% by Sanofi and 20% by Regeneron. If the Antibody Collaboration becomes profitable, Regeneron will be obligated to reimburse Sanofi for 50% of development expenses that were fully funded by Sanofi (or half of \$582.3 million as of December 31, 2011) and 30% of Shared Phase 3 Trial Costs, in accordance with a defined formula based on the amounts of these expenses and the Company's share of collaboration profits from commercialization of collaboration products. However, the Company is not required to apply more than 10% of its

share of the profits from the antibody collaboration in any calendar quarter to reimburse Sanofi for these development costs.

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

Sanofi will lead commercialization activities for products developed under the License Agreement, subject to the Company's right to co-promote such products. The parties will equally share profits and losses from sales within the United States. The parties will share profits outside the United States on a sliding scale based on sales starting at 65% (Sanofi)/35% (Regeneron) and ending at 55% (Sanofi)/45% (Regeneron), and losses outside the United States at 55% (Sanofi)/45% (Regeneron). In addition to profit sharing, the Company is entitled to receive up to \$250 million in sales milestone payments, with milestone payments commencing only if and after aggregate annual sales outside the United States exceed \$1.0 billion on a rolling 12-month basis.

Regeneron is obligated to use commercially reasonable efforts to supply clinical requirements of each drug candidate under the Antibody Collaboration until commercial supplies of that drug candidate are being manufactured. In connection with the November 2009 amendment of the collaboration's Discovery Agreement, Sanofi is funding up to \$30 million of agreed-upon costs incurred by the Company to expand its manufacturing capacity at the Company's Rensselaer, New York facilities, of which \$28.2 million has been received or is receivable at December 31, 2011.

With respect to each antibody product which enters development under the License Agreement, Sanofi or the Company may, by giving twelve months notice, opt-out of further development and/or commercialization of the product, in which event the other party retains exclusive rights to continue the development and/or commercialization of the product. The Company may also opt-out of the further development of an antibody product if it gives notice to Sanofi within thirty days of the date that Sanofi enters joint development of such antibody product under the License Agreement. Each of the Discovery Agreement and the License Agreement contains other termination provisions, including for material breach by the other party. Prior to December 31, 2017, Sanofi has the right to terminate the amended Discovery Agreement without cause with at least three months advance written notice; however, except under defined circumstances, Sanofi would be obligated to immediately pay to the Company the full amount of unpaid research funding during the remaining term of the research agreement through December 31, 2017. Upon termination of the collaboration in its entirety, the Company's obligation to reimburse Sanofi for development costs out of any future profits from collaboration products will terminate. Upon expiration of the amended Discovery Agreement, Sanofi has an option to license the Company's *VelocImmune*® technology for agreed upon consideration.

In connection with the Antibody Collaboration, in August 2008, the Company entered into a separate agreement with Sanofi to use Regeneron's proprietary *VelociGene*® technology platform to supply Sanofi with genetically modified mammalian models of gene function and disease (the *VelociGene*® Agreement). The *VelociGene*® Agreement provides for minimum annual order quantities for the term of the agreement, which extends through December 2012, for which the Company expects to receive payments totaling a minimum of \$21.5 million.

In accordance with the Company's revenue recognition policy described in Note 2, the (i) \$85.0 million up-front payment received in December 2007, (ii) reimbursement of Regeneron-incurred expenses under the Discovery and License Agreements, (iii) \$21.5 million of aggregate minimum payments under the *VelociGene*® Agreement, and (iv) reimbursement of agreed-upon costs to expand the Company's manufacturing capacity are being recognized as collaboration revenue over the related performance period. In connection with the amendments to expand and extend the Company's antibody collaboration with Sanofi, during the fourth quarter of 2009, the Company extended its estimated performance period related to the \$85.0 million up-front payment received from Sanofi under the Discovery Agreement and the \$21.5 million of aggregate minimum payments under the *VelociGene*® Agreement. The effect of this change in estimate resulted in the recognition of \$5.3 million less in collaboration revenue in both 2011 and 2010, compared to 2009.

In connection with the Antibody Collaboration, the Company recognized \$309.1 million, \$284.9 million, and \$210.7 million of collaboration revenue in 2011, 2010, and 2009, respectively. In addition, at December 31, 2011 and 2010, amounts receivable from Sanofi totaled \$78.5 million and \$75.7 million and deferred revenue was \$83.1 million and \$84.0 million, respectively.

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

***b. Bayer HealthCare LLC***

In October 2006, the Company entered into a license and collaboration agreement with Bayer HealthCare for the global development and commercialization outside the United States of EYLEA®. Under the terms of the agreement, Bayer HealthCare made a non-refundable up-front payment to the Company of \$75.0 million. In August 2007, the Company received a \$20.0 million milestone payment from Bayer HealthCare following dosing of the first patient in a Phase 3 study of EYLEA® in the neovascular form of wet AMD. In July 2009, the Company received a \$20.0 million substantive milestone payment from Bayer HealthCare following dosing of the first patient in a Phase 3 study of EYLEA® in central retinal vein occlusion ( CRVO ). In the fourth quarter of 2010, the Company earned two \$10.0 million substantive milestone payments (for a total of \$20.0 million) from Bayer HealthCare for achieving positive 52-week results in the Phase 3 study of EYLEA® in wet AMD and positive 6-month results in the Phase 3 study of EYLEA® in CRVO. One of these \$10.0 million payments was received in December 2010 and the other \$10.0 million payment was received in January 2011. The Company is eligible to receive up to \$50 million in future substantive milestone payments related to marketing approvals of EYLEA® in major market countries outside the United States. The Company is also eligible to receive up to \$135 million in sales milestone payments when and if total annual sales of EYLEA® outside the United States achieve certain specified levels starting at \$200 million.

The Company will share equally with Bayer HealthCare in any future profits arising from the commercialization of EYLEA® outside the United States. If EYLEA® is granted marketing authorization in a major market country outside the United States and the collaboration becomes profitable, the Company will be obligated to reimburse Bayer HealthCare out of its share of the collaboration profits for 50% of the agreed upon development expenses that Bayer HealthCare has incurred (or half of \$370.9 million as of December 31, 2011) in accordance with a formula based on the amount of development expenses that Bayer HealthCare has incurred and the Company's share of the collaboration profits, or at a faster rate at the Company's option. Within the United States, the Company is responsible for commercialization of EYLEA® and retains exclusive rights to any profits from such commercialization in the United States.

Starting in 2009, all agreed upon EYLEA® development expenses incurred by the Company and Bayer HealthCare, under a global development plan, are being shared equally. The Company is also obligated to use commercially reasonable efforts to supply clinical and commercial product requirements.

Bayer HealthCare has the right to terminate the Bayer 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, the Company retains all rights to EYLEA®.

The \$75.0 million up-front licensing payment and the \$20.0 million milestone payment received in August 2007 from Bayer HealthCare are being recognized as collaboration revenue over the related estimated performance period in accordance with the Company's revenue recognition policy as described in Note 2. In periods when the Company recognizes EYLEA® development expenses that the Company incurs under the collaboration, the Company also recognizes, as collaboration revenue, the portion of those EYLEA® development expenses that is reimbursable from Bayer HealthCare. In periods when Bayer HealthCare incurs agreed upon EYLEA® development expenses that benefit the collaboration and Regeneron, the Company also recognizes, as additional research and development expense, the portion of Bayer HealthCare's EYLEA® development expenses that the Company is obligated to reimburse.

The Company recognized \$43.1 million, \$75.4 million, and \$67.3 million of collaboration revenue from Bayer HealthCare in 2011, 2010, and 2009, respectively. In both 2010 and 2009, collaboration revenue from Bayer HealthCare included \$20.0 million in milestone payments, as described above, which, for the purpose of revenue recognition, were considered substantive. In addition, in 2011, 2010, and 2009, the Company recognized as additional research and development expense \$47.8 million, \$48.9 million, and \$37.7 million, respectively, of EYLEA® development expenses that the Company was obligated to reimburse to Bayer HealthCare.

In connection with cost-sharing of EYLEA® expenses under the collaboration, \$4.5 million was receivable from Bayer HealthCare at December 31, 2011 and \$2.3 million was payable to Bayer HealthCare at December 31, 2010. In addition, at December 31, 2011 and 2010, deferred revenue from the Company's collaboration with Bayer HealthCare was \$42.4 million and \$47.0 million, respectively.

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

**c. National Institute of Health**

In September 2006, the Company was awarded a grant from the National Institutes of Health ( NIH ) as part of the NIH 's Knockout Mouse Project. As amended, the NIH grant provided a minimum of \$25.3 million in funding over a five-year period, including \$1.5 million in funding to optimize certain existing technology, subject to compliance with its terms and annual funding approvals, for the Company 's use of its *VelociGene*® technology to generate a collection of targeting vectors and targeted mouse embryonic stem cells which can be used to produce knockout mice. The Company records revenue in connection with the NIH grant using a proportional performance model as it incurs expenses related to the grant, subject to the grant 's terms and annual funding approvals. In 2011, 2010, and 2009, the Company recognized contract research revenue of \$3.6 million, \$4.6 million, and \$5.5 million, respectively, from the NIH Grant. As of the end of 2011, no further revenue will be recognized by the Company in connection with this NIH Grant.

**4. Technology Licensing Agreements**

In March 2007, the Company entered into a six-year, non-exclusive license agreement with Astellas Pharma Inc. to allow Astellas to utilize the Company 's *VelocImmune*® technology in its internal research programs to discover human monoclonal antibodies. Under the terms of the agreement, Astellas made a \$20.0 million annual, non-refundable payment to the Company in each of 2010, 2009, 2008, and 2007. In July 2010, the license agreement with Astellas was amended and extended through June 2023. Under the terms of the amended agreement, Astellas made a \$165.0 million up-front payment to the Company in August 2010, which was deferred upon receipt and will be recognized as revenue ratably over the seven-year period beginning in mid-2011. In addition, Astellas will make a \$130.0 million second payment to the Company in June 2018 unless the license agreement has been terminated prior to that date. Astellas has the right to terminate the agreement at any time by providing 90 days ' advance written notice. Under certain limited circumstances, such as a material breach of the agreement by the Company, Astellas may terminate the agreement and receive a refund of a portion of its up-front payment or, if such termination occurs after June 2018, a portion of its second payment, to the Company under the July 2010 amendment to the agreement. The Company is entitled to receive a mid-single digit royalty on any future sales of antibody products discovered by Astellas using the Company 's *VelocImmune*® technology. In connection with the Astellas license agreement, for each of the years ended December 31, 2011, 2010, and 2009, the Company recognized \$22.0 million, \$20.0 million, and \$20.0 million of technology licensing revenue, respectively. In addition, deferred revenue at December 31, 2011 and 2010 was \$151.7 million and \$173.7 million, respectively.

In February 2007, the Company entered into a six-year, non-exclusive license agreement with AstraZeneca UK Limited to allow AstraZeneca to utilize the Company 's *VelocImmune*® technology in its internal research programs to discover human monoclonal antibodies. Under the terms of the agreement, AstraZeneca made a \$20.0 million annual, non-refundable payment to the Company in each of 2010, 2009, 2008, and 2007. Each annual payment was deferred and recognized as revenue ratably over approximately the ensuing twelve-month period. In November 2010, as permitted by the agreement, MedImmune Limited (as successor by novation from AstraZeneca) gave written notice of voluntary termination of the agreement, effective in February 2011, thereby canceling its obligation to make either of the final two annual payments. Regeneron remains entitled to receive mid-single digit royalties on any future sales of antibody products discovered by MedImmune/AstraZeneca using the *VelocImmune*® technology. In connection with the AstraZeneca license agreement, for the years ended December 31, 2011, 2010, and 2009, the Company recognized \$2.9 million, \$20.0 million, and \$20.0 million, respectively, of technology licensing revenue.

**5. Product Revenue**

In November 2011, the Company received marketing approval from the FDA for EYLEA® for the treatment of wet AMD. In accordance with the Company 's revenue recognition policy described in Note 2, the Company recorded EYLEA® net product sales of \$24.8 million for the year ended December 31, 2011.

In February 2008, the Company received marketing approval from the FDA for ARCALYST® Injection for Subcutaneous Use for the treatment of CAPS. ARCALYST® net product sales totaled \$19.9 million, \$25.3 million, and \$18.4 million for the years ended December 31, 2011, 2010, and 2009, respectively. The Company had limited historical returns experience for ARCALYST® beginning with initial sales in 2008 through the end of 2009; therefore, ARCALYST® net product sales were deferred until the right of return no longer existed and rebates could be reasonably estimated. Effective in the first quarter of 2010, the Company determined that it had accumulated sufficient historical data to reasonably estimate both product returns and rebates of ARCALYST®. As a result, ARCALYST® net product sales during 2010 included

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\$20.5 million of net product sales made during this period and \$4.8 million of previously deferred net product sales. The effect of recognizing the previously deferred ARCALYST® net product sales revenue was to lower the Company's net loss per share by \$0.06 in 2010.

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**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

**6. Marketable Securities**

Marketable securities at December 31, 2011 and 2010 consisted of debt securities, as detailed below, and equity securities. The aggregate fair value of the equity securities was \$3.0 million and \$3.6 million at December 31, 2011 and 2010, respectively, and the aggregate cost basis was \$4.0 million at both December 31, 2011 and 2010. The Company also held restricted marketable securities at both December 31, 2011 and December 31, 2010, which consisted of debt securities, as detailed below, that collateralize letters of credit and lease obligations.

The following tables summarize the amortized cost basis of debt securities included in marketable securities, the aggregate fair value of those securities, and gross unrealized gains and losses on those securities at December 31, 2011 and 2010. The Company classifies its debt securities, other than mortgage-backed securities, based on their contractual maturity dates. Maturities of mortgage-backed securities have been estimated based primarily on repayment characteristics and experience of the senior tranches that the Company holds.

<b>At December 31, 2011</b>	<b>Amortized Cost Basis</b>	<b>Fair Value</b>	<b>Unrealized</b>		<b>Net</b>
			<b>Gains</b>	<b>(Losses)</b>	
<i>Unrestricted</i>					
Maturities within one year					
U.S. government obligations	\$ 12,025	\$ 12,067	\$ 42		\$ 42
U.S. government guaranteed corporate bonds	15,263	15,316	53		53
U.S. government guaranteed collateralized mortgage obligations	623	622		(1)	(1)
Municipal bonds	15,314	15,326	13	(1)	12
	43,225	43,331	108	(2)	106
Maturities after one year through five years					
U.S. government obligations	272,433	272,752	400	(81)	319
Mortgage-backed securities	104	28		(76)	(76)
	272,537	272,780	400	(157)	243
Maturities after five years through ten years					
Mortgage-backed securities	164	87		(77)	(77)
	315,926	316,198	508	(236)	272
<i>Restricted</i>					
Maturities within one year					
U.S. government obligations	3,347	3,357	10		10
Maturities after one year through five years					
U.S. government obligations	2,572	2,583	11		11
	5,919	5,940	21		21
	\$ 321,845	\$ 322,138	\$ 529	\$ (236)	\$ 293



**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

At December 31, 2010	Amortized Cost Basis	Fair Value	Unrealized Gains	(Losses)	Net
<i>Unrestricted</i>					
Maturities within one year					
U.S. government obligations	\$ 83,635	\$ 83,684	\$ 54	\$ (5)	\$ 49
U.S. government guaranteed corporate bonds	48,173	48,531	358		358
U.S. government guaranteed collateralized mortgage obligations	2,027	2,131	104		104
Municipal bonds	1,597	1,603	6		6
Mortgage-backed securities	875	847		(28)	(28)
	136,307	136,796	522	(33)	489
Maturities after one year through five years					
U.S. government obligations	352,345	350,683	64	(1,726)	(1,662)
U.S. government guaranteed corporate bonds	15,522	15,477		(45)	(45)
Mortgage-backed securities	110	38		(72)	(72)
	367,977	366,198	64	(1,843)	(1,779)
Maturities after five years through ten years					
Mortgage-backed securities	284	243		(41)	(41)
	504,568	503,237	586	(1,917)	(1,331)
<i>Restricted</i>					
Maturities within one year					
U.S. government obligations	2,922	2,921		(1)	(1)
Maturities after one year through five years					
U.S. government obligations	4,135	4,118		(17)	(17)
	7,057	7,039		(18)	(18)
	\$ 511,625	\$ 510,276	\$ 586	\$ (1,935)	\$ (1,349)

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

At December 31, 2011 and 2010, marketable securities included an additional unrealized loss of \$1.0 million and \$0.4 million, respectively, related to one equity security in the Company's marketable securities portfolio.

The following table shows the fair value of the Company's marketable securities that have unrealized losses and that are deemed to be only temporarily impaired, aggregated by investment category and length of time that the individual securities have been in a continuous unrealized loss position, at December 31, 2011 and 2010. The debt securities listed at December 31, 2011, excluding mortgage-backed securities, mature at various dates through December 2014. The mortgage-backed securities listed at December 31, 2011 mature at various dates through April 2018.

	Less than 12 Months		12 Months or Greater		Total	
	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss
<b>At December 31, 2011</b>						
<i>Unrestricted</i>						
U.S. government obligations	\$ 103,529	\$ (81)			\$ 103,529	\$ (81)
U.S. government guaranteed collateralized mortgage obligations	623	(1)			623	(1)
Municipal bonds	4,603	(1)			4,603	(1)
Equity security	3,019	(1,025)			3,019	(1,025)
Mortgage-backed securities			\$ 116	\$ (152)	116	(152)
	\$ 111,774	\$ (1,108)	\$ 116	\$ (152)	\$ 111,890	\$ (1,260)
<b>At December 31, 2010</b>						
<i>Unrestricted</i>						
U.S. government obligations	\$ 340,444	\$ (1,731)			\$ 340,444	\$ (1,731)
U.S. government guaranteed corporate bonds	19,005	(45)			19,005	(45)
Equity security	3,612	(433)			3,612	(433)
Mortgage-backed securities			\$ 1,128	\$ (141)	1,128	(141)
	363,061	(2,209)	1,128	(141)	364,189	(2,350)
<i>Restricted</i>						
U.S. government obligations	6,154	(18)			6,154	(18)
	6,154	(18)			6,154	(18)
	\$ 369,215	\$ (2,227)	\$ 1,128	\$ (141)	\$ 370,343	\$ (2,368)

Realized gains and losses are included as a component of investment income. For the years ended December 31, 2011, 2010, and 2009, total realized gains and losses on sales of marketable securities were not material. In computing realized gains and losses, the Company computes the cost of its investments on a specific identification basis. Such cost includes the direct costs to acquire the security, adjusted for the amortization of any discount or premium.

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

The Company's assets that are measured at fair value on a recurring basis, at December 31, 2011 and 2010, were as follows:

	Fair Value	Fair Value Measurements at Reporting Date		
		Using Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
<b>At December 31, 2011</b>				
<i>Unrestricted</i>				
Available-for-sale marketable securities				
U.S. government obligations	\$ 284,819		\$ 284,819	
U.S. government guaranteed corporate bonds	15,316		15,316	
U.S. government guaranteed collateralized mortgage obligations	622		622	
Municipal bonds	15,326		15,326	
Mortgage-backed securities	115		115	
Equity security	3,019	\$ 3,019		
	319,217	3,019	316,198	
<i>Restricted</i>				
Available-for-sale marketable securities				
U.S. government obligations	5,940		5,940	
	\$ 325,157	\$ 3,019	\$ 322,138	
<b>At December 31, 2010</b>				
<i>Unrestricted</i>				
Available-for-sale marketable securities				
U.S. government obligations	\$ 434,367		\$ 434,367	
U.S. government guaranteed corporate bonds	64,008		64,008	
U.S. government guaranteed collateralized mortgage obligations	2,131		2,131	
Municipal bonds	1,603		1,603	
Mortgage-backed securities	1,128		1,128	
Equity security	3,612	\$ 3,612		
	506,849	3,612	503,237	
<i>Restricted</i>				

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Available-for-sale marketable  
securities

U.S. government obligations	7,039	7,039
	\$ 513,888	\$ 3,612
		\$ 510,276

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**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

Marketable securities included in Level 2 were valued using a market approach utilizing prices and other relevant information, such as interest rates, yield curves, prepayment speeds, loss severities, credit risks, and default rates, generated by market transactions involving identical or comparable assets. The Company considers market liquidity in determining the fair value for these securities. During the year ended December 31, 2010, deterioration in the credit quality of a marketable security subjected the Company to the risk of not being able to recover the carrying value of these securities. As a result, the Company recognized a \$0.1 million impairment charge related to its Level 2 marketable securities in 2010, which the Company considered to be other-than-temporarily impaired. The Company did not record any charges for other-than-temporary impairment of its Level 2 marketable securities in 2011 and 2009.

The Company held one Level 3 marketable security, which had a fair value of \$0 at December 31, 2011 and 2010. This Level 3 security was valued using information provided by the Company's investment advisors and other sources, including quoted bid prices which took into consideration the securities' lack of liquidity. In 2009, the Company recorded a charge of \$0.1 million for other-than-temporary impairment of this Level 3 marketable security; therefore, as of December 31, 2009, the fair value of this security had been written down to zero. There were no purchases, sales, or maturities of Level 3 marketable securities and no unrealized gains or losses related to Level 3 marketable securities for the years ended December 31, 2011 and 2010. There were no transfers of marketable securities between Levels 1, 2, or 3 classifications during the years ended December 31, 2011 and 2010.

## 7. Inventory

Inventories as of December 31, 2011 and December 31, 2010 consist of the following:

	2011	2010
Raw materials	\$ 1,608	\$ 592
Work in process	10,806	699
Finished goods	1,142	132
	\$ 13,556	\$ 1,423

At December 31, 2011, \$3.5 million of inventories were included in prepaid expenses and other current assets and \$10.1 million of inventories were included in other assets. At December 31, 2010, inventories were included in prepaid expenses and other current assets.

In 2011, cost of goods sold included inventory write-downs of \$0.5 million. In 2010, there were no inventory write-downs included in cost of goods sold.

## 8. Property, Plant, and Equipment

Property, plant, and equipment as of December 31, 2011 and 2010 consist of the following:

	2011	2010
Land	\$ 2,117	\$ 2,117
Building and improvements	322,753	242,035
Leasehold improvements	4,479	4,063
Construction-in-progress	10,880	70,356
Laboratory and other equipment	156,397	137,951
Furniture, computer and office equipment, and other	29,468	22,235
	526,094	478,757
Less, accumulated depreciation and amortization	(158,139)	(131,307)
	\$ 367,955	\$ 347,450

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Depreciation and amortization expense on property, plant, and equipment amounted to \$31.1 million, \$19.7 million, and \$14.2 million for the years ended December 31, 2011, 2010, and 2009, respectively. Effective in the first quarter of 2010, the estimated useful lives of certain capitalized laboratory and other equipment, which is a component of property, plant, and equipment, were extended. The effect of this change in estimate was to lower depreciation expense by \$4.0 million and to lower the Company's net loss per share by \$0.05 for the year ended December 31, 2010.

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**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

Included in property, plant, and equipment at December 31, 2011 and December 31, 2010 was \$3.6 million and \$2.8 million, respectively, of leased equipment under capital leases, and related accumulated amortization was \$0.5 million and \$0.1 million at December 31, 2011 and December 31, 2010, respectively.

Property, plant, and equipment at both December 31, 2011 and 2010 includes \$86.2 million of costs incurred by the Company's landlord to construct new laboratory and office facilities in Tarrytown, New York in connection with the Company's December 2006 lease, as amended, of these facilities. See Note 12a.

The Company capitalized interest costs of \$6.4 million in 2010. The Company did not capitalize any interest costs in 2011.

### 9. Accounts Payable and Accrued Expenses

Accounts payable and accrued expenses as of December 31, 2011 and 2010 consist of the following:

	2011	2010
Accounts payable	\$ 27,736	\$ 15,589
Accrued payroll and related costs	42,835	12,025
Accrued clinical trial expense	9,850	9,727
Accrued property, plant, and equipment costs	1,070	7,622
Other accrued expenses and liabilities	14,134	6,441
Payable to Bayer HealthCare		2,254
	<u>\$ 95,625</u>	<u>\$ 53,658</u>

### 10. Deferred Revenue

Deferred revenue as of December 31, 2011 and 2010 consists of the following:

	2011	2010
<b>Current portion:</b>		
Received from Sanofi (see Note 3a)	\$ 20,011	\$ 19,506
Received from Bayer HealthCare (see Note 3b)	7,907	9,884
Received for technology license agreements (see Note 4)	23,572	25,008
Other	150	325
	<u>\$ 51,640</u>	<u>\$ 54,723</u>
<b>Long-term portion:</b>		
Received from Sanofi (see Note 3a)	\$ 86,017	\$ 97,081
Received from Bayer HealthCare (see Note 3b)	34,456	37,067
Received for technology license agreements (see Note 4)	128,137	151,708
	<u>\$ 248,610</u>	<u>\$ 285,856</u>

### 11. Convertible Debt

In October 2011, the Company issued \$400.0 million aggregate principal amount of 1.875% convertible senior notes (the "Notes") in a private placement. The net proceeds from the Notes offering were \$391.1 million after deducting the initial purchaser's discount and issuance costs.





**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

The Notes will pay interest semi-annually on April 1 and October 1, beginning April 1, 2012, and will mature on October 1, 2016 unless earlier converted or repurchased. The Notes will be convertible, subject to certain conditions, into cash, shares of the Company's Common Stock, or a combination of cash and shares of Common Stock, at the Company's option. The initial conversion rate for the Notes will be 11.9021 shares of Common Stock (subject to adjustment in certain circumstances) per \$1,000 principal amount of the Notes, or a total of approximately 4,760,840 shares upon conversion, which is equal to an initial conversion price of approximately \$84.02 per share. A holder of the Notes may surrender their Notes at their option any time prior to the close of business on the business day immediately preceding July 1, 2016, only under the following circumstances: (i) during any calendar quarter commencing after the calendar quarter ending on December 31, 2011 (and only during such calendar quarter), if the last reported sale price of the Company's Common Stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the conversion price on each applicable trading day; (ii) during the five business day period after any ten consecutive trading day period (the "measurement period") in which the trading price, as defined, of the Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of the Company's Common Stock and the conversion rate on each such trading day; (iii) if the Company elects to issue to all or substantially all holders of its Common Stock any rights, options or warrants (other than pursuant to a rights plan) entitling them for a period of not more than 60 calendar days after the record date for such issuance, to subscribe for or purchase shares of the Company's Common Stock, at a price per share less than the average of the last reported sales prices of the Company's Common Stock for the ten consecutive day period ending on, and including, the trading day immediately preceding the declaration date for such issuance; (iv) upon specified distributions to the Company's shareholders; or (v) upon the occurrence of specified corporate transactions, such as a fundamental change (i.e., a change in control), or the Company's Common Stock ceasing to be listed on at least one U.S. national securities exchange. On or after July 1, 2016, holders may convert their Notes at the conversion rate at any time prior to the close of business on the second scheduled trading day immediately preceding the maturity date irrespective of the foregoing conditions. In the event that a fundamental change, as defined in the indenture under which the Notes have been issued, occurs prior to maturity of the Notes, the initial conversion rate may be increased to include additional shares upon conversion, or holders can require the Company to purchase from them all or a portion of their Notes for 100% of the principal value plus any accrued and unpaid interest.

The Company has reserved sufficient shares of its Common Stock to satisfy the conversion requirements related to the Notes. The Company may not redeem the Notes prior to their maturity date.

In accordance with accounting guidance for debt with conversion and other options, the Company accounted for the liability and equity components of the Notes separately. The estimated fair value of the liability component at the date of issuance was \$271.1 million, and was computed based on the fair value of similar debt instruments that do not include a conversion feature. The equity component of \$120.9 million was recognized as a debt discount and represents the difference between the \$392.0 million of gross proceeds from the issuance of the Notes and the \$271.1 million estimated fair value of the liability component at the date of issuance. The debt discount is amortized over the expected life of a similar liability without the equity component. The Company determined this expected life to be equal to the term of the Notes, resulting in an amortization period ending October 1, 2016. The effective interest rate used to amortize the debt discount is approximately 10.2%, which was based on the Company's estimated non-convertible borrowing rate as of the date the Notes were issued.

Issuance costs of \$0.9 million related to the issuance of the Notes were allocated to the liability and equity components in proportion to the allocation of the proceeds and accounted for as capitalized debt issuance costs and equity issuance costs, respectively.

The net carrying amount of the liability component of the Notes as of December 31, 2011 consists of the following:

	<b>2011</b>
Total convertible senior notes par	\$ 400,000
Unamortized discount	(124,981)
	<u>\$ 275,019</u>

Total interest expense associated with the Notes consisted of the following for the year ended December 31, 2011:

	<b>2011</b>
Contractual coupon interest rate	\$ 1,455

<u>Amortization of discount and note issuance costs</u>	3,944
	\$5,399

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
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As of December 31, 2011, the "if converted value" did not exceed the principal amount of the Notes since the closing sales price of the Company's Common Stock was less than the initial conversion price of the Notes. The fair value of the outstanding Notes was estimated to be \$375.5 million as of December 31, 2011, and was determined based on quoted market rates.

In connection with the offering of the Notes, the Company entered into convertible note hedge ( call option ) and warrant transactions with multiple counterparties, including an affiliate of the initial purchaser. The convertible note hedge transactions cover, subject to customary anti-dilution adjustments, the number of shares of the Company's Common Stock that initially underlie the Notes, and are intended to reduce the potential dilutive impact of the conversion feature of the Notes. The convertible note hedge will terminate upon the earlier of the maturity date of the Notes or the first day the Notes are no longer outstanding. The Company paid \$117.5 million for the convertible note hedge, which was recorded as a reduction to additional paid-in capital.

The warrant transactions have an initial strike price of approximately \$103.41 per share, and may be settled in cash or shares of the Company's Common Stock, at the Company's option. The warrant transactions will have a dilutive effect to the extent that the market price per share of the Company's Common Stock exceeds the applicable strike price of the warrants. Proceeds received from the warrant transactions totaled \$93.8 million and were recorded as additional paid-in capital. The warrants expire at various dates during 2017.

The convertible note hedge and warrants are both considered indexed to the Company's Common Stock and classified as equity; therefore, the convertible note hedge and warrants are not accounted for as derivative instruments. The Company has reserved sufficient shares of its Common Stock to satisfy the potential settlement of the warrants.

## **12. Commitments and Contingencies**

### ***a. Leases***

#### *Descriptions of Lease Agreements*

The Company leases laboratory and office facilities in Tarrytown, New York, under a December 2006 lease agreement, as amended (the Tarrytown Lease ). The facilities leased by the Company under the Tarrytown Lease include (i) space in previously existing buildings, (ii) newly constructed space in two new buildings ( Buildings A and B ) that was completed in the third quarter of 2009 and, (iii) under a December 2009 amendment to the Tarrytown Lease, additional newly constructed space in a third new building ( Building C ) that was completed in the first quarter of 2011. The Tarrytown Lease will expire in June 2024 and contains three renewal options to extend the term of the lease by five years each, escalations at 2.5% per annum, and early termination options for various portions of the space exclusive of the newly constructed space in Buildings A and B. The Tarrytown Lease provides for monthly payments over its term and additional charges for utilities, taxes, and operating expenses. Certain premises under the Tarrytown Lease are accounted for as operating leases. However, for Buildings A, B, and C that the Company is leasing, the Company is deemed, in substance, to be the owner of the landlord's buildings in accordance with the application of FASB authoritative guidance, and the landlord's costs of constructing these new facilities are required to be capitalized on the Company's books as a non-cash transaction, offset by a corresponding lease obligation on the Company's balance sheet.

In connection with the Tarrytown Lease, the Company issued a letter of credit in the amount of \$3.4 million and collateralized the letter of credit with cash and marketable debt securities totaling \$3.6 million at both December 31, 2011 and 2010. Such collateral has been classified as restricted cash and marketable securities.

In October 2008, the Company entered into a sublease with Sanofi U.S. for office space in Bridgewater, New Jersey. The lease commenced in January 2009 and expired in July 2011. In July 2011, the Company entered into an operating lease for office space in Liberty Corner, New Jersey, which expires in January 2017.

The Company also leases certain equipment under operating and capital leases which expire at various times through 2014.

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
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*Commitments under Operating Leases*

The estimated future minimum noncancelable lease commitments under operating leases were as follows:

<b>December 31,</b>	<b>Facilities</b>	<b>Equipment</b>	<b>Total</b>
2012	\$ 6,072	\$ 1,188	\$ 7,260
2013	7,304	258	7,562
2014	7,428	35	7,463
2015	7,583		7,583
2016	7,738		7,738
Thereafter	59,631		59,631
	<b>\$ 95,756</b>	<b>\$ 1,481</b>	<b>\$ 97,237</b>

Rent expense under operating leases was:

<b>Year Ending December 31,</b>	<b>Facilities</b>	<b>Equipment</b>	<b>Total</b>
2011	\$ 7,191	\$ 599	\$ 7,790
2010	7,301	335	7,636
2009	7,722	395	8,117

In addition to its rent expense under operating leases, and payments under facility lease obligations (see below), for various facilities, the Company paid rental charges for utilities, real estate taxes, and operating expenses of \$9.3 million, \$10.3 million, and \$8.4 million for the years ended December 31, 2011, 2010, and 2009, respectively.

*Commitments under Capital Leases*

In 2011 and 2010, the Company entered into capital leases in connection with acquisitions of new equipment. The lease obligations are collateralized with marketable debt securities totaling \$3.3 million and \$3.5 at December 31, 2011 and 2010, respectively; such collateral has been classified as restricted cash and marketable securities at December 31, 2011 and 2010.

The estimated future minimum noncancelable lease commitments under capital leases were as follows:

<b>December 31,</b>	<b>Equipment</b>
2012	\$ 1,394
2013	1,254
2014	130
Total minimum lease payments	2,778
Less: amount representing interest	(272)
	<b>\$ 2,506</b>

At the end of the lease term, the Company is required to purchase the leased equipment for a nominal amount defined in the lease agreement. At December 31, 2011 and 2010, capital lease obligations totaled \$2.5 million and \$2.8 million, respectively, and were included in other liabilities.

*Facility Lease Obligations*

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As described above, in connection with the application of FASB authoritative guidance to the Company's lease of office and laboratory facilities in Buildings A, B, and C, the Company capitalized the landlord's costs of constructing the new facilities and recognized a corresponding facility lease obligation. The Company also recognized, as additional facility lease obligation, reimbursements from the Company's landlord for tenant improvement costs that the Company incurred since, under FASB authoritative guidance, such payments that the Company receives from its landlord are deemed to be a financing obligation. Monthly lease payments on these facilities are allocated between the land element of the lease (which is accounted for as an operating lease) and the facility lease obligation, based on the estimated relative fair values of the land and buildings.

As of December 31, 2010, the Company had capitalized the landlord's costs of constructing Buildings A and B, which totaled \$58.4 million, and of constructing Building C, which totaled \$27.8 million. Reimbursements from the Company's landlord for Buildings A and B tenant improvement costs totaled \$56.9 million and were received by the Company during 2010 and 2009. Reimbursements for Building C tenant improvement costs totaled \$14.2 million and were received by the Company during 2010. With respect to Buildings A and B, monthly lease payments commenced in August 2009, the buildings were placed in service by the Company in September 2009, and the imputed interest rate applicable to the Company's facility lease obligation is approximately 11%. With respect to Building C, monthly lease payments commenced in January 2011, the building was placed in service by the Company in February 2011, and the imputed interest rate applicable to the Company's facility lease obligation is approximately 9%.

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**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

In 2011, the Company recognized \$15.6 million of interest expense in connection with the Buildings A and B and the Building C facility lease obligations. In 2010 and 2009, the Company recognized \$9.1 million and \$2.3 million, respectively, of interest expense in connection with the Buildings A and B facility lease obligation. At December 31, 2011 and 2010, the Buildings A and B facility lease obligation balance was \$113.0 million and \$113.7 million, respectively, and the Building C facility lease obligation balance was \$47.5 million and \$46.4 million, respectively.

The estimated future minimum noncancelable commitments under these facility lease obligations, as of December 31, 2011, were as follows:

December 31,	Buildings A and B	Building C	Total
2012	\$ 12,847	\$ 2,825	\$ 15,672
2013	13,092	4,370	17,462
2014	13,343	4,490	17,833
2015	13,600	4,614	18,214
2016	13,864	4,740	18,604
Thereafter	113,040	39,899	152,939
	\$ 179,786	\$ 60,938	\$ 240,724

**b. Research Collaboration and Licensing Agreements**

As part of the Company's research and development efforts, the Company enters into research collaboration and licensing agreements with related and unrelated companies, scientific collaborators, universities, and consultants. These agreements contain varying terms and provisions which include fees and milestones to be paid by the Company, services to be provided, and ownership rights to certain proprietary technology developed under the agreements. Some of the agreements contain provisions which require the Company to pay royalties, as defined, at rates that range from 0.25% to 16.5%, in the event the Company sells or licenses any proprietary products developed under the respective agreements.

In December 2011, the Company and Genentech, Inc., a member of the Roche Group, entered into a Non-Exclusive License and Partial Settlement Agreement (the Genentech Agreement) relating to ophthalmic sales of EYLEA<sup>®</sup> in the United States. Pursuant to the Genentech Agreement, the Company received a non-exclusive license to certain patents relating to VEGF receptor proteins, known as the Davis-Smyth patents, and other technology patents. The Davis-Smyth patents are the subject of patent litigation between the Company and Genentech now pending in the United States District Court, Southern District of New York. Patent litigation is continuing with respect to matters not covered by the Genentech Agreement (see Note 18).

Under the terms of the Genentech Agreement, the Company agreed to make payments to Genentech based on U.S. sales of EYLEA<sup>®</sup> commencing upon FDA approval of EYLEA<sup>®</sup> in November 2011 through May 7, 2016. The Company will be required to make a one-time, non-refundable \$60 million payment upon cumulative U.S. sales of EYLEA<sup>®</sup> reaching \$400 million. In addition, the Company agreed to pay royalties of 4.75% on cumulative U.S. sales of EYLEA<sup>®</sup> between \$400 million and \$3 billion and 5.5% on any cumulative U.S. sales of EYLEA<sup>®</sup> over \$3 billion. As the Company records net product sales of EYLEA<sup>®</sup>, the Company is recognizing expense in connection with the Genentech Agreement using a blended mid-single digit royalty rate that reflects both the \$60 million payment and the royalties payable on cumulative sales and that is based upon the Company's estimate of cumulative EYLEA<sup>®</sup> sales through May 7, 2016.

The Company recognizes royalty expense based on net product sales of EYLEA<sup>®</sup> and ARCALYST<sup>®</sup> under various licensing agreements, including, for EYLEA<sup>®</sup>, the Genentech Agreement described above. For the years ended December 31, 2011, 2010, and 2009, royalties on net product sales totaled \$3.2 million, \$1.7 million, and \$1.5 million, respectively, and are included in cost of goods sold.

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**

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

In July 2008, the Company and Collectis S.A. ( Collectis ) entered into an Amended and Restated Non-Exclusive License Agreement (the Collectis Agreement ). The Collectis Agreement resolved a dispute between the parties related to the interpretation of a license agreement entered into by the parties in December 2003 pursuant to which the Company licensed certain patents and patent applications from Collectis. Pursuant to the Collectis Agreement, in July 2008, the Company made a non-refundable \$12.5 million payment to Collectis (the Collectis Payment ) and agreed to pay Collectis a low single-digit royalty based on revenue received by the Company from any future licenses or sales of the Company's *VelociGene*<sup>®</sup> or *VelocImmune*<sup>®</sup> products and services. No royalties are payable to Collectis with respect to the Company's *VelocImmune*<sup>®</sup> license agreements with AstraZeneca and Astellas or the Company's antibody collaboration with Sanofi. Moreover, no royalties are payable to Collectis on any revenue from commercial sales of antibodies from the Company's *VelocImmune*<sup>®</sup> technology.

The Company began amortizing the Collectis Payment in the second quarter of 2008 in proportion to past and future anticipated revenues under the Company's license agreements with AstraZeneca and Astellas and the Discovery and Preclinical Development Agreement under the Company's antibody collaboration with Sanofi (as amended in November 2009). In 2011, 2010, and 2009, the Company recognized \$1.0 million, \$0.9 million, and \$2.3 million, respectively, of expense in connection with the Collectis Payment. At December 31, 2011 and 2010, the unamortized balance of the Collectis Payment, which was included in other assets, was \$5.7 million and \$6.6 million, respectively. The Company estimates that it will recognize expense of \$1.0 million in each of 2012 and 2013, and \$0.9 million in each of 2014, 2015, and 2016, in connection with the Collectis Payment.

### **13. Stockholders' Equity**

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

In September 2003, Sanofi purchased 2,799,552 newly issued, unregistered shares of the Company's Common Stock for \$45.0 million. See Note 3.

In December 2007, Sanofi purchased 12 million newly issued, unregistered shares of the Company's Common Stock for an aggregate cash price of \$312.0 million. As a condition to the closing of this transaction, Sanofi entered into an investor agreement with the Company, which was amended in November 2009. Under the amended investor agreement, Sanofi has three demand rights to require the Company to use all reasonable efforts to conduct a registered underwritten public offering with respect to shares of the Company's Common Stock beneficially owned by Sanofi immediately after the closing of the transaction. Until the later of the fifth anniversaries of the expiration or earlier termination of the License and Collaboration Agreement, as amended in 2009, under the Company's antibody collaboration with Sanofi (see Note 3) and the Company's collaboration agreement with Sanofi for the development and commercialization of ZALTRAP<sup>®</sup> (see Note 3), Sanofi will be bound by certain standstill provisions. These provisions include an agreement not to acquire more than a specified percentage of the outstanding shares of the Company's Class A Stock and Common Stock. The percentage increased from 25% to 30% as of December 20, 2011. Under the amended investor agreement, Sanofi has also agreed not to dispose of any shares of the Company's Common Stock that were beneficially owned by Sanofi immediately after the closing of the transaction until December 20, 2017, subject to certain limited exceptions. Following December 20, 2017, Sanofi will be permitted to sell shares of the Company's Common Stock (i) in a registered underwritten public offering undertaken pursuant to the demand registration rights granted to Sanofi and described above, subject to the underwriter's broad distribution of securities sold, (ii) pursuant to Rule 144 under the Securities Act and transactions exempt from registration under the Securities Act, subject to a volume limitation of one million shares of the Company's Common Stock every three months and a prohibition on selling to beneficial owners, or persons that would become beneficial owners as a result of such sale, of 5% or more of the outstanding shares of the Company's Common Stock, and (iii) into an issuer tender offer, or a tender offer by a third party that is recommended or not opposed by the Company's board of directors. Sanofi has agreed to vote, and cause its affiliates to vote, all shares of the Company's voting securities they are entitled to vote, at Sanofi's election, either as recommended by the Company's board of directors or proportionally with the votes cast by the Company's other shareholders, except with respect to certain change of control transactions, liquidation or dissolution, stock issuances equal to or exceeding 10% of the then outstanding shares or voting rights of the Company's Class A Stock and Common Stock, and new equity compensation plans or amendments if not materially consistent with the Company's historical equity compensation practices. The rights and restrictions under the investor agreement are subject to

termination upon the occurrence of certain events.

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**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
*(Unless otherwise noted, dollars in thousands, except per share data)*

In October 2010, the Company completed an underwritten public offering of 6,325,000 shares of Common Stock and received net proceeds of \$174.8 million. Sanofi purchased 1,017,401 shares of Common Stock in this offering.

In October 2011, the Company completed a private placement of \$400.0 million aggregate principal amount of Notes, which are convertible into shares of the Company's Common Stock. In accordance with accounting guidance for debt with conversion and other options, the Company accounted for the liability and equity components of the Notes separately. The equity component of the Notes was \$120.6 million, net of issuance costs. In connection with the offering of the Notes, the Company entered into convertible note hedge and warrant transactions. The Company paid \$117.5 million for the convertible note hedge, which was recorded as a reduction to additional paid-in capital. The warrant transactions have an initial strike price of approximately \$103.41 per share, and may be settled in cash or shares of the Company's Common Stock, at the Company's option. Proceeds received from the warrant transactions totaled \$93.8 million and were recorded as additional paid-in capital. The warrants expire at various dates during 2017. See Note 11.

#### **14. Long-Term Incentive Plans**

During 2000, the Company established the Regeneron Pharmaceuticals, Inc. 2000 Long-Term Incentive Plan which, as amended and restated (the 2000 Incentive Plan), provides for the issuance of up to 41,307,016 shares of Common Stock in respect of awards. Employees of the Company, including officers, and nonemployees, including consultants and nonemployee members of the Company's board of directors, (collectively, Participants) may receive awards as determined by a committee of independent directors (Committee). The awards that may be made under the 2000 Incentive Plan include: (a) Incentive Stock Options (ISOs) and Nonqualified Stock Options, (b) shares of Restricted Stock, (c) shares of Phantom Stock, (d) Stock Bonuses, and (e) Other Awards.

Stock Option awards grant Participants the right to purchase shares of Common Stock at prices determined by the Committee; however, in the case of an ISO, the option exercise price will not be less than the fair market value of a share of Common Stock on the date the Option is granted. Options vest over a period of time determined by the Committee, generally on a pro rata basis over a three to five year period. The Committee also determines the expiration date of each Option; however, no ISO is exercisable more than ten years after the date of grant. The maximum term of options that have been awarded under the 2000 Incentive Plan is ten years.

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

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

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
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Other Awards are other forms of awards which are valued based on the Company's Common Stock. Subject to the provisions of the 2000 Incentive Plan, the terms and provisions of such Other Awards are determined solely on the authority of the Committee.

The 2000 Incentive Plan contains provisions that allow for the Committee to provide for the immediate vesting of awards upon a change in control of the Company, as defined in the plan.

As of December 31, 2011, there were 10,244,318 shares available for future grants under the 2000 Incentive Plan.

*a. Stock Options*

Transactions involving stock option awards during 2011 under the 2000 Incentive Plan is summarized in the table below.

	Number of Shares	Weighted- Average Exercise Price	Weighted- Average Remaining Contractual Term (in years)	Intrinsic Value (in thousands)
<b>Stock Options:</b>				
Outstanding at December 31, 2010	23,362,248	\$ 19.93		
<b>2011:</b>				
Granted	4,286,640	\$ 51.96		
Forfeited	(247,898)	\$ 28.11		
Expired	(551,456)	\$ 13.31		
Exercised	(4,523,173)	\$ 18.73		
Outstanding at December 31, 2011	22,326,361	\$ 26.40	6.90	\$ 663,376
Vested and expected to vest at December 31, 2011	21,755,141	\$ 26.04	6.84	\$ 653,990
Exercisable at December 31, 2011	11,963,345	\$ 18.27	5.27	\$ 451,478

The Company satisfies stock option exercises with newly issued shares of the Company's Common Stock. The total intrinsic value of stock options exercised during 2011, 2010, and 2009 was \$49.2 million, \$21.4 million, and \$13.2 million, respectively. The intrinsic value represents the amount by which the market price of the underlying stock exceeds the exercise price of an option.

The Company grants stock options with exercise prices that are equal to or greater than the average market price of the Company's Common Stock on the date of grant (Market Price). The table below summarizes the weighted-average exercise prices and weighted-average grant-date fair values of options issued during the years ended December 31, 2011, 2010, and 2009. The fair value of each option granted under the 2000 Incentive Plan during 2011, 2010, and 2009 was estimated on the date of grant using the Black-Scholes option-pricing model.

	Number of Options Granted	Weighted- Average Exercise Price	Weighted- Average Fair Value
<b>2011:</b>			
Exercise price equal to Market Price	4,286,640	\$ 51.96	\$ 23.82
<b>2010:</b>			
Exercise price equal to Market Price	4,319,856	\$ 29.43	\$ 13.36

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<b>2009:</b>				
Exercise price equal to Market Price	3,490,560	\$	20.69	\$ 10.89

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**NOTES TO FINANCIAL STATEMENTS (Continued)**  
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For the years ended December 31, 2011, 2010, and 2009, the Company recognized \$39.2 million, \$29.4 million, and \$27.4 million, respectively, of non-cash stock-based compensation expense related to non-performance based stock option awards. As of December 31, 2011, there was \$93.6 million of stock-based compensation cost related to outstanding non-performance based stock options, net of estimated forfeitures, which had not yet been recognized. The Company expects to recognize this compensation cost over a weighted-average period of 1.9 years.

In addition, there were 2,195,429 performance-based options which were outstanding and unvested as of December 31, 2011 of which, subject to the optionee satisfying certain service conditions, 203,429 options that were issued in 2005 would vest upon achieving certain defined sales targets for the Company's products and 1,992,000 options that were issued in 2011, 2010, and 2009 would vest upon achieving certain development milestones for the Company's product candidates. In light of the Company's receipt of marketing approval for EYLEA® for the treatment of wet AMD in November 2011, and the status of the Company's development programs at December 31, 2011, the Company estimates that all of the remaining performance-based options issued in 2005, 2009, and 2010 will vest and approximately 50% of the performance-based options issued in 2011 will vest.

For the years ended December 31, 2011 and 2010, the Company recognized \$11.7 million and \$8.1 million, respectively, of non-cash stock-based compensation expense related to these performance options. As of December 31, 2011 there was \$17.4 million of stock-based compensation cost which had not yet been recognized related to the performance based options that the Company currently estimates will vest. The Company expects to recognize this compensation cost over a weighted-average period of 2.5 years. In addition, potential compensation cost of \$10.2 million related to the performance options issued in 2011, whose performance conditions (based on current facts and circumstances) are not currently considered by the Company to be probable of attainment, will begin to be recognized only if and when the Company estimates that it is probable that these options will vest. The Company's estimates of the number of performance-based options that will vest will be revised, if necessary, in subsequent periods. Changes in these estimates may materially affect the amount of stock-based compensation recognized in future periods related to performance-based options.

Fair value Assumptions:

The following table summarizes the weighted average values of the assumptions used in computing the fair value of option grants during 2011, 2010, and 2009.

	2011	2010	2009
Expected volatility	48%	47%	54%
Expected lives from grant date	6.1 years	5.6 years	5.9 years
Expected dividend yield	0%	0%	0%
Risk-free interest rate	1.31%	2.11%	2.87%

Expected volatility has been estimated based on actual movements in the Company's stock price over the most recent historical periods equivalent to the options' expected lives. Expected lives are principally based on the Company's historical exercise experience with previously issued employee and board of directors' option grants. The expected dividend yield is zero as the Company has never paid dividends and does not currently anticipate paying any in the foreseeable future. The risk-free interest rates are based on quoted U.S. Treasury rates for securities with maturities approximating the options' expected lives.

*b. Restricted Stock*

A summary of the Company's activity related to Restricted Stock awards for the year ended December 31, 2011 is summarized below:

<u>Restricted Stock:</u>	Number of Shares	Weighted- Average Grant Date Fair Value
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Outstanding at December 31, 2010		845,000	\$ 25.37
<b>2011:</b>	Granted	16,500	\$ 58.59
	Released	(110,001)	\$ 30.63
	Outstanding at December 31, 2011	751,499	\$ 25.33

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**REGENERON PHARMACEUTICALS, INC.**  
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The Company recognized non-cash stock-based compensation expense from Restricted Stock awards of \$5.7 million, \$2.4 million, and \$2.2 million in 2011, 2010, and 2009, respectively. As of December 31, 2011, there were 751,499 unvested shares of Restricted Stock outstanding and \$9.8 million of stock-based compensation cost related to these unvested shares which had not yet been recognized. The Company expects to recognize this compensation cost over a weighted-average period of 1.4 years.

**15. Executive Stock Purchase Plan**

In 1989, the Company adopted an Executive Stock Purchase Plan (the Plan) under which 1,027,500 shares of Class A Stock were reserved for restricted stock awards. The Plan provides for the compensation committee of the board of directors to award employees, directors, consultants, and other individuals (Plan participants) who render service to the Company the right to purchase Class A Stock at a price set by the compensation committee. The Plan provides for the vesting of shares as determined by the compensation committee and, should the Company's relationship with a Plan participant terminate before all shares are vested, unvested shares will be repurchased by the Company at a price per share equal to the original amount paid by the Plan participant. During 1989 and 1990, a total of 983,254 shares were issued, all of which vested as of December 31, 1999. As of December 31, 2011, there were 44,246 shares available for future grants under the Plan.

**16. Employee Savings Plan**

In 1993, the Company adopted the provisions of the Regeneron Pharmaceuticals, Inc. 401(k) Savings Plan (the Savings Plan). The terms of the Savings Plan provide for employees who have met defined service requirements to participate in the Savings Plan by electing to contribute to the Savings Plan a percentage of their compensation to be set aside to pay their future retirement benefits, as defined. The Savings Plan, as amended and restated, provides for the Company to make discretionary contributions (Contribution), as defined. The Company recognized \$4.1 million, \$3.2 million, and \$2.6 million of Contribution expense in 2011, 2010, and 2009, respectively. At December 31, 2011 and 2010, accrued Contribution expense totaled \$3.6 million and \$2.9 million, respectively. During the first quarter of 2012 and 2011, the Company contributed 63,937 and 91,761 shares, respectively, of Common Stock to the Savings Plan in satisfaction of these obligations.

**17. Income Taxes**

For the year ended December 31, 2011, the Company incurred a net loss for tax purposes and recognized a full valuation allowance against deferred taxes. In 2011, the Company recognized a \$1.1 million income tax benefit, consisting of (i) \$0.7 million related to tax legislation that allowed the Company to claim a refund for a portion of its unused pre-2006 research tax credits and (ii) \$0.4 million in connection with the net tax effect of the change in the Company's unrealized gain (loss) on available-for-sale marketable securities, which is included in other comprehensive income (loss).

For the year ended December 31, 2010, the Company incurred a net loss for tax purposes and recognized a full valuation allowance against deferred taxes. No provision or benefit for income taxes was recognized by the Company in 2010.

For the year ended December 31, 2009, the Company incurred a net loss for tax purposes and recognized a full valuation allowance against deferred taxes. In 2009, the Company recognized a \$4.1 million income tax benefit, consisting of (i) \$2.7 million resulting from tax legislation that allowed the Company to claim a refund of U.S. federal alternative minimum tax (AMT) that the Company paid in connection with its 2007 U.S. federal income tax return, (ii) \$0.7 million resulting from tax legislation that allowed the Company to claim a refund for a portion of its unused pre-2006 research tax credits on its 2009 U.S. federal income tax return, and (iii) \$0.7 million in connection with the net tax effect of the Company's unrealized gain on available-for-sale marketable securities, which is included in other comprehensive income in 2009.

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**NOTES TO FINANCIAL STATEMENTS (Continued)**  
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The tax effect of temporary differences, net operating loss carry-forwards, and research and experimental and other tax credit carry-forwards as of December 31, 2011 and 2010 is as follows:

	2011	2010
<b>Deferred tax assets:</b>		
Net operating loss carry-forward	\$ 282,480	\$ 243,893
Fixed assets	14,847	13,600
Deferred revenue	120,490	70,443
Deferred compensation	47,092	39,120
Research and experimental and other tax credit carry-forwards	67,734	45,588
Capitalized research and development costs	31,371	38,865
Other	15,956	10,863
	579,790	462,372
<b>Deferred tax liabilities:</b>		
Convertible senior notes	(1,428)	
<b>Net deferred tax assets</b>	<b>578,542</b>	
Valuation allowance	(578,542)	(462,372)
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The Company's valuation allowance increased by \$116.2 million in 2011, due primarily to increases in the Company's net operating loss carry-forward and tax credit carry-forwards and the full recognition of the \$165.0 million up-front payment received from Astellas in 2010 as taxable income in 2011. The Company's valuation allowance increased by \$63.0 million in 2010, due primarily to increases in the net operating loss carry-forward and tax credit carry-forwards.

The Company is primarily subject to U.S. federal and New York State income taxes. The difference between the Company's effective income tax rate and the U.S. federal statutory rate of 35% is primarily attributable to an increase in the deferred tax valuation allowance. In 2011 and early 2012, U.S. federal tax authorities concluded examinations of the Company's 2007, 2008, and 2009 federal income tax returns. The Company's 2010 federal income tax return is currently being examined by the U.S. federal tax authorities. In addition, tax years subsequent to 2007 remain open to examination by New York State tax authorities.

As of December 31, 2011 and 2010, the Company had no accruals for interest or penalties related to income tax matters.

As of December 31, 2011, the Company had available for tax purposes unused net operating loss carry-forwards of \$800.2 million which will expire in various years from 2018 to 2031 and included \$96.2 million of net operating loss carry-forwards related to exercises of Nonqualified Stock Options and disqualifying dispositions of Incentive Stock Options, the tax benefit from which, if realized, will be credited to additional paid-in capital. The Company's research and experimental and other tax credit carry-forwards expire in various years from 2012 to 2031. Under the Internal Revenue Code and similar state provisions, substantial changes in the Company's ownership have resulted in an annual limitation on the amount of net operating loss and tax credit carry-forwards that can be utilized in future years to offset future taxable income. This annual limitation may result in the expiration of net operating losses and tax credit carry-forwards before utilization.

The following table summarizes the gross amounts of unrecognized tax benefits at the beginning and end of 2011 and 2010:

	2011	2010
Balance as of January 1	\$ 12,819	\$ -
Gross increases related to current year tax positions	2,192	3,550
Gross increases related to prior year tax positions		9,269
Gross decreases due to settlements	(9,415)	
Balance as of December 31	\$ 5,596	\$ 12,819





**REGENERON PHARMACEUTICALS, INC.**  
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In 2011, the gross decrease in unrecognized tax benefits related to prior year tax positions was primarily due to the conclusion of examinations of the Company's 2007, 2008, and 2009 federal income tax returns by U.S. federal tax authorities. In 2010, the gross increases in unrecognized tax benefits related to prior year tax positions was primarily due to the Company's calculations of certain pre-2010 tax credits. Due to the amounts of the Company's net operating loss carry-forward and tax credit carry-forwards, the Company has not accrued interest or penalties related to these unrecognized tax benefits. In addition, unrecognized tax benefits at December 31, 2011 and 2010, if recognized, would not affect the Company's effective tax rate since the adjustments to deferred tax assets would be fully offset by adjustments to the Company's valuation allowance. For the year ended December 31, 2009, income tax positions that were deemed uncertain under the recognition thresholds and measurement attributes prescribed in FASB authoritative guidance were not material.

### 18. Legal Matters

From time to time, the Company is a party to legal proceedings in the course of the Company's business. The Company does not expect any such current ordinary course legal proceedings to have a material adverse effect on the Company's business or financial condition. Costs associated with the Company's involvement in legal proceedings are expensed as incurred.

#### *Genentech Patent Litigation*

The Company is aware of issued patents and pending patent applications owned by Genentech that claim certain chimeric VEGF receptors. The Company does not believe that ZALTRAP® or EYLEA® infringe any valid claim in these patents or patent applications. The Company is involved in five patent litigations with Genentech, two in the United States and three in Europe. In November 2010, the Company commenced a lawsuit against Genentech in the U.S. District Court for the Southern District of New York (the Court), seeking a declaratory judgment that no activities relating to the Company's VEGF Trap infringe any valid claim of certain Genentech patents referred to as the Davis-Smyth patents (the First Davis-Smyth Case). Genentech answered the complaint and asserted counterclaims that the Company's prior or planned activities relating to VEGF Trap have infringed or will infringe claims of four of the five Davis-Smyth patents and requested a judgment against the Company for damages, including for willful infringement, and other relief as the Court deems appropriate.

On December 31, 2011, the Company entered into a Non-Exclusive License and Partial Settlement Agreement with Genentech that covers making, using, and selling EYLEA® in the United States for the prevention and treatment of human eye diseases and disorders in the United States. Under the Genentech Agreement, the Company received a non-exclusive license to the Davis-Smyth patents, and certain other technology patents owned or co-owned by Genentech. The Genentech Agreement does not cover any non-U.S. patent rights or non-U.S. patent disputes, and does not cover any use of aflibercept other than for prevention and treatment of human eye diseases and disorders in the United States. The First Davis-Smyth Case is continuing with respect to matters not covered by the Genentech Agreement. The Genentech Agreement provides for the Company to make payments to Genentech based on U.S. sales of EYLEA® through May 7, 2016, the date the Davis-Smyth patents expire. The Company will make a lump-sum payment of \$60 million once cumulative U.S. sales of EYLEA® reach \$400 million. The Company will also pay royalties of 4.75% on cumulative U.S. sales of EYLEA® between \$400 million and \$3 billion and 5.5% on any cumulative U.S. sales of EYLEA® over \$3 billion. As a result of the Genentech Agreement, on January 17, 2012 Genentech filed a second amended answer and counterclaim in the First Davis-Smyth Case, in which it amended its counterclaims alleging infringement of four of the five Davis-Smyth patents. On December 23, 2011, Genentech initiated a related case in the Court against Regeneron and Sanofi alleging infringement of four of the five Davis-Smyth Patents by activities relating to VEGF Trap (but excluding EYLEA®) (the Second Davis-Smyth Case). As in the First Davis-Smyth Case, in the new complaint Genentech requests a judgment against the Company for damages, including for willful infringement, and other relief as the Court deems appropriate.

The Company believes Genentech's claims in the First Davis Smyth Case and the Second Davis Smyth Case are without merit and intend to continue to defend against all of Genentech's remaining claims vigorously. As this litigation is at an early stage, at this time the Company is not able to predict the probability of the outcome or an estimate of loss, if any, related to these matters.

The Company has initiated patent-related actions against Genentech in Germany, the United Kingdom, and Italy, and may initiate other actions in other countries outside the United States, which could have similar or other adverse outcomes that would materially harm its business and which, irrespective of the outcomes, may also entail significant costs and expenses.

**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
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**19. Net Loss Per Share Data**

The Company's basic net loss per share amounts have been computed by dividing net loss by the weighted average number of Common and Class A shares outstanding. Net loss per share is presented on a combined basis, inclusive of Common Stock and Class A Stock outstanding, as each class of stock has equivalent economic rights. In 2011, 2010, and 2009, the Company reported net losses; therefore, no common stock equivalents were included in the computation of diluted net loss per share since such inclusion would have been antidilutive. The calculations of basic and diluted net loss per share are as follows:

	December 31,		
	2011	2010	2009
Net loss (Numerator)	\$ (221,760)	\$ (104,468)	\$ (67,830)
Weighted-average shares, in thousands (Denominator)	90,610	82,926	79,782
Basic and diluted net loss per share	\$ (2.45)	\$ (1.26)	\$ (0.85)

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

	December 31,		
	2011	2010	2009
<b>Options:</b>			
Weighted average number, in thousands	20,942	21,428	20,040
Weighted average exercise price	\$ 21.21	\$ 18.80	\$ 17.66
<b>Restricted Stock:</b>			
Weighted average number, in thousands	846	526	500
<b>Convertible Senior Notes:</b>			
Weighted average number, in thousands	939		
<b>Warrants:</b>			
Weighted average number, in thousands	939		

**20. Statement of Cash Flows**

Supplemental disclosure of noncash investing and financing activities:

Included in accounts payable and accrued expenses at December 31, 2011, 2010, and 2009 were \$6.2 million, \$10.7 million, and \$9.8 million of accrued capital expenditures, respectively.

Pursuant to the application of FASB authoritative guidance to the Company's lease of office and laboratory facilities in Tarrytown, New York (see Note 12a), the Company recognized a facility lease obligation of \$0.2 million and \$31.7 million during 2010 and 2009, respectively, in connection with capitalizing, on the Company's books, the landlord's costs of constructing new facilities that the Company has leased. The Company did not recognize any such facility lease obligations during 2011.

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Included in facility lease obligations and property, plant, and equipment at December 31, 2010 was \$3.7 million of capitalized and deferred interest for the year ended December 31, 2010, as the related facilities being leased by the Company were under construction and lease payments on these facilities did not commence until January 2011. For the years ended December 31, 2011 and 2009, the Company did not capitalize any interest.

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**REGENERON PHARMACEUTICALS, INC.**  
**NOTES TO FINANCIAL STATEMENTS (Continued)**  
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The Company incurred capital lease obligations of \$0.7 and \$2.9 million during 2011 and 2010 in connection with acquisitions of new equipment.

Included in marketable securities at December 31, 2011, 2010, and 2009 were \$0.7 million, \$1.4 million, and \$0.6 million of accrued interest income, respectively.

**21. Unaudited Quarterly Results**

Summarized quarterly financial data for the years ended December 31, 2011 and 2010 are set forth in the following tables.

	<b>First Quarter Ended March 31, 2011 (Unaudited)</b>	<b>Second Quarter Ended June 30, 2011</b>	<b>Third Quarter Ended September 30, 2011</b>	<b>Fourth Quarter Ended December 31, 2011</b>
Revenues	\$ 112,204	\$ 107,810	\$ 102,833	\$ 122,977
Net loss	(43,447)	(62,505)	(62,365)	(53,443)
Net loss per share, basic and diluted	\$ (0.49)	\$ (0.69)	\$ (0.68)	\$ (0.58)

	<b>First Quarter Ended March 31, 2010 (Unaudited)</b>	<b>Second Quarter Ended June 30, 2010</b>	<b>Third Quarter Ended September 30, 2010</b>	<b>Fourth Quarter Ended December 31, 2010</b>
Revenues	\$ 103,534	\$ 115,886	\$ 105,979	\$ 133,675
Net loss	(30,522)	(25,474)	(33,875)	(14,597)
Net loss per share, basic and diluted	\$ (0.38)	\$ (0.31)	\$ (0.41)	\$ (0.17)