



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

Form 10-Q

(Mark One)

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

For the quarterly period ended March 31, 2008

OR

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

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission File Number 0-19034

**REGENERON PHARMACEUTICALS, INC.**

(Exact name of registrant as specified in its charter)

New York

(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) 347-7000

(Registrant's telephone number, including area code)

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 is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See 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   
(Do not check if a 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

Indicate the number of shares outstanding of each of the issuer's classes of common stock as of April 15, 2008:

Class of Common Stock	Number of Shares
Class A Stock, \$0.001 par value	2,257,698
Common Stock, \$0.001 par value	76,848,479

**REGENERON PHARMACEUTICALS, INC.**  
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**March 31, 2008**

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	March 31, 2008	December 31, 2007
<b>ASSETS</b>		
Current assets		
Cash and cash equivalents	\$ 520,875	\$ 498,925
Marketable securities	222,373	267,532
Accounts receivable from the sanofi-aventis Group	31,100	14,244
Accounts receivable — other	1,860	4,076
Prepaid expenses and other current assets	11,297	13,052
Total current assets	<u>787,505</u>	<u>797,829</u>
Restricted cash	1,600	1,600
Marketable securities	83,010	78,222
Property, plant, and equipment, at cost, net of accumulated depreciation and amortization	58,419	58,304
Other assets	342	303
Total assets	<u>\$ 930,876</u>	<u>\$ 936,258</u>
<b>LIABILITIES and STOCKHOLDERS' EQUITY</b>		
Current liabilities		
Accounts payable and accrued expenses	\$ 30,314	\$ 39,232
Deferred revenue from sanofi-aventis, current portion	18,855	18,855
Deferred revenue — other, current portion	36,785	25,577
Notes payable	200,000	200,000
Total current liabilities	<u>285,954</u>	<u>283,664</u>
Deferred revenue from sanofi-aventis	121,718	126,431
Deferred revenue — other	62,601	65,896
Total liabilities	<u>470,273</u>	<u>475,991</u>
Commitments and contingencies		
Stockholders' equity		
Preferred stock, \$.01 par value; 30,000,000 shares authorized; issued and outstanding—none		
Class A Stock, convertible, \$.001 par value; 40,000,000 shares authorized; shares issued and outstanding - 2,257,698 in 2008 and 2,260,266 in 2007	2	2
Common Stock, \$.001 par value; 160,000,000 shares authorized; shares issued and outstanding - 76,838,871 in 2008 and 76,592,218 in 2007	77	77
Additional paid-in capital	1,264,531	1,253,235
Accumulated deficit	(804,835)	(793,217)
Accumulated other comprehensive income	828	170
Total stockholders' equity	<u>460,603</u>	<u>460,267</u>
Total liabilities and stockholders' equity	<u>\$ 930,876</u>	<u>\$ 936,258</u>

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

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**REGENERON PHARMACEUTICALS, INC.**  
**CONDENSED STATEMENTS OF OPERATIONS (Unaudited)**  
*(In thousands, except per share data)*

	<b>Three months ended March 31,</b>	<b>2007</b>
	<b>2008</b>	<b>2007</b>
<b>Revenues</b>		
Contract research and development from sanofi-aventis	\$ 35,734	\$ 11,830
Other contract research and development	10,649	1,815
Technology licensing	10,000	2,143
	<u>56,383</u>	<u>15,788</u>
<b>Expenses</b>		
Research and development	61,270	41,235
Selling, general, and administrative	11,024	8,202
	<u>72,294</u>	<u>49,437</u>
Loss from operations	<u>(15,911)</u>	<u>(33,649)</u>
<b>Other income (expense)</b>		
Investment income	7,304	6,743
Interest expense	(3,011)	(3,011)
	<u>4,293</u>	<u>3,732</u>
Net loss	<u>\$ (11,618)</u>	<u>\$ (29,917)</u>
Net loss per share, basic and diluted	\$ (0.15)	\$ (0.46)
Weighted average shares outstanding, basic and diluted	78,493	65,563

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

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**REGENERON PHARMACEUTICALS, INC.**  
**CONDENSED STATEMENT OF STOCKHOLDERS' EQUITY (Unaudited)**  
**For the three months ended March 31, 2008**  
**(In thousands)**

	Class A Stock		Common Stock		Additional Paid-in Capital	Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Equity	Comprehensive Loss
	Shares	Amount	Shares	Amount					
<b>Balance, December 31, 2007</b>	<u>2,260</u>	<u>\$ 2</u>	<u>76,592</u>	<u>\$ 77</u>	<u>\$ 1,253,235</u>	<u>\$ (793,217)</u>	<u>\$ 170</u>	<u>\$ 460,267</u>	
Issuance of Common Stock in connection with exercise of stock options, net of shares tendered			186		1,903			1,903	
Issuance of Common Stock in connection with Company 401(k) Savings Plan contribution			59		1,107			1,107	
Conversion of Class A Stock to Common Stock	(2)		2						
Stock-based compensation expense					8,286			8,286	
Net loss						(11,618)		(11,618)	\$ (11,618)
Change in net unrealized gain on marketable securities							658	658	658
<b>Balance, March 31, 2008</b>	<u>2,258</u>	<u>\$ 2</u>	<u>76,839</u>	<u>\$ 77</u>	<u>\$ 1,264,531</u>	<u>\$ (804,835)</u>	<u>\$ 828</u>	<u>\$ 460,603</u>	<u>\$ (10,960)</u>

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

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**REGENERON PHARMACEUTICALS, INC.**  
**CONDENSED STATEMENTS OF CASH FLOWS (Unaudited)**  
*(In thousands)*

	<b>Three months ended March 31,</b>	
	<b>2008</b>	<b>2007</b>
<b>Cash flows from operating activities</b>		
Net loss	\$ (11,618)	\$ (29,917)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization	2,946	2,855
Non-cash compensation expense	8,286	6,585
Changes in assets and liabilities		
Increase in accounts receivable	(14,640)	(26,139)
Decrease (increase) in prepaid expenses and other assets	1,493	(440)
Increase in deferred revenue	3,200	37,666
(Decrease) increase in accounts payable, accrued expenses, and other liabilities	(7,564)	152
Total adjustments	(6,279)	20,679
Net cash used in operating activities	(17,897)	(9,238)
<b>Cash flows from investing activities</b>		
Purchases of marketable securities	(91,518)	(186,177)
Sales or maturities of marketable securities	132,509	113,262
Capital expenditures	(3,047)	(1,197)
Net cash provided by (used in) investing activities	37,944	(74,112)
<b>Cash flows from financing activities</b>		
Net proceeds from the issuance of Common Stock	1,903	1,958
Net cash provided by financing activities	1,903	1,958
Net increase (decrease) in cash and cash equivalents	21,950	(81,392)
Cash and cash equivalents at beginning of period	498,925	237,876
Cash and cash equivalents at end of period	\$ 520,875	\$ 156,484

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

**REGENERON PHARMACEUTICALS, INC.**

**Notes to Condensed Financial Statements (Unaudited)**

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

**1. Interim Financial Statements**

The interim Condensed Financial Statements of Regeneron Pharmaceuticals, Inc. (“Regeneron” or the “Company”) have been prepared in accordance with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all information and disclosures necessary for a presentation of the Company’s financial position, results of operations, and cash flows in conformity with accounting principles generally accepted in the United States of America. In the opinion of management, these financial statements reflect all adjustments, consisting only of normal recurring accruals, necessary for a fair presentation of the Company’s financial position, results of operations, and cash flows for such periods. The results of operations for any interim periods are not necessarily indicative of the results for the full year. The December 31, 2007 Condensed Balance Sheet data were derived from audited financial statements, but do not include all disclosures required by accounting principles generally accepted in the United States of America. These financial statements should be read in conjunction with the financial statements and notes thereto contained in the Company’s Annual Report on Form 10-K for the year ended December 31, 2007.

**2. ARCALYST™ (rilonacept) Product Revenue and Inventory**

***Product Revenue***

In late March 2008, ARCALYST™ (rilonacept) became available for prescription in the United States for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS) and the Company made its first shipments of ARCALYST™ to its distributors. The Company will recognize revenue from product sales in accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition* (“SAB 104”). Revenue from product sales is recognized when persuasive evidence of an arrangement exists, title to product and associated risk of loss has passed to the customer, the price is fixed or determinable, collection from the customer is reasonably assured and we have no further performance obligations. When recognized, revenues from product sales will be recorded net of applicable provisions for prompt pay discounts, product returns, and estimated rebates. The Company will account for these reductions in accordance with Emerging Issues Task Force Issue No. 01-9, *Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor’s Products)* (“EITF 01-9”), and Statement of Financial Accounting Standards No. (“SFAS”) 48, *Revenue Recognition When Right of Return Exists*, as applicable.

Since the Company has no historical return or rebate experience for ARCALYST™, no product sales revenue has been recognized in the first quarter of 2008, and revenue recognition has been fully deferred until the right of return no longer exists and rebates have been processed, or until the Company can reasonably estimate returns and rebates. At March 31, 2008, deferred revenue related to ARCALYST™ product sales totaled \$0.8 million.



[Table of Contents](#)**REGENERON PHARMACEUTICALS, INC.****Notes to Condensed Financial Statements (Unaudited)***(Unless otherwise noted, dollars in thousands, except per share data)***Inventory**

The Company began capitalizing inventory costs associated with commercial supplies of ARCALYST™ (rilonacept) subsequent to receipt of marketing approval from the U.S. Food and Drug Administration ("FDA") on February 27, 2008. Costs for manufacturing supplies of ARCALYST™ prior to receipt of FDA approval were recognized as research and development expenses in the period incurred; therefore, these costs will not be included in cost of goods sold when those supplies of ARCALYST™ are sold. At March 31, 2008, inventoried costs related to ARCALYST™ were insignificant.

**3. Per Share Data**

The Company's basic and diluted net loss per share amounts have been computed by dividing net loss by the weighted average number of shares of Common Stock and Class A Stock 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. For the three months ended March 31, 2008 and 2007, the Company reported net losses; therefore, no common stock equivalents were included in the computation of diluted net loss per share for these periods, since such inclusion would have been antidilutive. The calculations of basic and diluted net loss per share are as follows:

	Three Months Ended March 31,	
	2008	2007
Net loss (Numerator)	\$(11,618)	\$(29,917)
Weighted-average shares, in thousands (Denominator)	78,493	65,563
Basic and diluted net loss per share	\$ (0.15)	\$ (0.46)

Shares issuable upon the exercise of stock options, vesting of restricted stock awards, and conversion of convertible debt, which have been excluded from the March 31, 2008 and 2007 diluted per share amounts because their effect would have been antidilutive, include the following:

	Three months ended March 31,	
	2008	2007
Stock Options:		
Weighted average number, in thousands	17,680	15,549
Weighted average exercise price	\$ 17.16	\$ 15.65
Restricted Stock:		
Weighted average number, in thousands	500	
Convertible Debt:		
Weighted average number, in thousands	6,611	6,611
Conversion price	\$ 30.25	\$ 30.25

**REGENERON PHARMACEUTICALS, INC.**

**Notes to Condensed Financial Statements (Unaudited)**

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

**4. Statement of Cash Flows**

Supplemental disclosure of noncash investing and financing activities:

In the first quarter of 2008, the Company recognized \$0.6 million of compensation expense related to Restricted Stock awards, the fair value of which is expensed, on a pro rata basis, over the period that the restrictions on the shares lapse.

Included in accounts payable and accrued expenses at March 31, 2008 and December 31, 2007 were \$1.5 million and \$1.7 million, respectively, of accrued capital expenditures. Included in accounts payable and accrued expenses at March 31, 2007 and December 31, 2006 were \$0.6 million and \$0.8 million, respectively, of accrued capital expenditures.

Included in accounts payable and accrued expenses at December 31, 2007 and 2006 were \$1.1 million and \$1.4 million, respectively, of accrued Company 401(k) Savings Plan contribution expense. In the first quarter of 2008 and 2007, the Company contributed 58,575 and 64,532 shares, respectively, of Common Stock to the 401(k) Savings Plan in satisfaction of these obligations.

Included in marketable securities at March 31, 2008 and December 31, 2007 were \$2.1 million and \$2.2 million, respectively, of accrued interest income. Included in marketable securities at March 31, 2007 and December 31, 2006 were \$2.1 million and \$1.5 million, respectively, of accrued interest income.

**5. Fair Value of Financial Assets**

***Adoption of Statement of Financial Accounting Standards No. 157***

In September 2006, the Financial Accounting Standards Board issued SFAS 157, *Fair Value Measurements*. SFAS 157 defines fair value, establishes a framework for measuring fair value in accordance with accounting principles generally accepted in the United States, and expands disclosures about fair value measurements. The Company adopted the provisions of SFAS 157 as of January 1, 2008, for financial instruments. Although the adoption of SFAS 157 did not materially impact the Company's financial condition, results of operations, or cash flows, the Company is now required to provide additional disclosures as part of its financial statements.

SFAS 157 establishes 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.

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The Company's assets that are measured at fair value on a recurring basis, and subject to the disclosure requirements of SFAS 157 at March 31, 2008, were as follows:

Description	Fair Value at March 31, 2008	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)
Available-for-sale marketable securities	\$305,383		\$297,433	\$7,950

Marketable securities included in Level 2 above were valued using a market approach utilizing prices and other relevant information generated by market transactions involving identical or comparable assets.

Marketable securities included in Level 3 above were valued using information provided by the Company's investment advisors, including quoted bid prices which take into consideration the securities' current lack of liquidity. There were no realized or unrealized gains or losses related to the Company's Level 3 marketable securities for the three months ended March 31, 2008. In addition, there were no purchases, sales, or maturities of Level 3 marketable securities, and no transfers of marketable securities between the Level 2 and Level 3 classifications, during the quarter ended March 31, 2008. The Company held no Level 1 marketable securities during the quarter.

**6. Accounts Receivable**

Accounts receivable as of March 31, 2008 and December 31, 2007 consist of the following:

	March 31, 2008	December 31, 2007
Receivable from the sanofi-aventis Group	\$ 31,100	\$ 14,244
Receivable from Bayer HealthCare LLC		2,797
Other	1,860	1,279
	<u>\$ 32,960</u>	<u>\$ 18,320</u>

[Table of Contents](#)**REGENERON PHARMACEUTICALS, INC.****Notes to Condensed Financial Statements (Unaudited)***(Unless otherwise noted, dollars in thousands, except per share data)***7. Accounts Payable and Accrued Expenses**

Accounts payable and accrued expenses as of March 31, 2008 and December 31, 2007 consist of the following:

	March 31, 2008	December 31, 2007
Accounts payable	\$ 9,475	\$ 8,128
Payable to Bayer HealthCare	1,053	4,892
Accrued payroll and related costs	6,460	14,514
Accrued clinical trial expense	4,221	5,609
Accrued expenses, other	4,063	3,797
Interest payable on convertible notes	5,042	2,292
	<u>\$ 30,314</u>	<u>\$ 39,232</u>

**8. Comprehensive Loss**

The Company presents comprehensive income (loss) in accordance with SFAS 130, *Reporting Comprehensive Income*. Comprehensive loss of the Company includes net loss adjusted for the change in net unrealized gain (loss) on marketable securities. The net effect of income taxes on comprehensive loss is immaterial. For the three months ended March 31, 2008 and 2007, the components of comprehensive loss are:

	Three months ended March 31, 2008	2007
Net loss	\$ (11,618)	\$ (29,917)
Change in net unrealized gain (loss) on marketable securities	658	72
Total comprehensive loss	<u>\$ (10,960)</u>	<u>\$ (29,845)</u>

**9. Legal Matters**

In December 2003, the Company entered into a non-exclusive license agreement with Collectis Inc. that granted the Company certain rights in a family of patents relating to homologous recombination. Collectis now claims that the Company's use of *VelocImmune*<sup>®</sup> and the Company's agreements with AstraZeneca UK Limited, Astellas Pharma Inc., and sanofi-aventis are outside the scope of the Company's license from Collectis. As a result, Collectis claims that it has terminated the Company's non-exclusive license agreement and has requested that the Company cease and desist from using the patents licensed from Collectis. The Company disagrees with Collectis' position

**REGENERON PHARMACEUTICALS, INC.**

**Notes to Condensed Financial Statements (Unaudited)**

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

and is in discussions with Cellectis regarding this matter. If the Company is not able to resolve this dispute, Cellectis may commence a lawsuit against the Company, sanofi-aventis, the Company's *VelocImmune* licensees, and the Company's *VelociGene*<sup>®</sup> customers alleging infringement of the patents the Company licensed from Cellectis. The Company is unable to estimate the losses or expenses, if any, that may result from the resolution of this matter; however, such losses or expenses could be material.

**10. Future Impact of Recently Issued Accounting Standards**

In November 2007, the Emerging Issues Task Force issued Statement No. 07-1, *Accounting for Collaborative Arrangements* ("EITF 07-1"). EITF 07-01 defines collaborative arrangements and establishes reporting requirements for transactions between participants in a collaborative arrangement and between participants in the arrangement and third parties. EITF 07-1 also establishes the appropriate income statement presentation and classification for joint operating activities and payments between participants, as well as the sufficiency of the disclosures related to these arrangements. EITF 07-1 is effective for fiscal years beginning after December 15, 2008, and will be applied retrospectively as a change in accounting principle for collaborative arrangements existing at the effective date. The Company is required to adopt EITF 07-1 for the fiscal year beginning January 1, 2009. Management does not anticipate that the adoption of EITF 07-1 will have a material impact on the Company's financial statements.

## Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

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

### Overview

Regeneron Pharmaceuticals, Inc. is a biopharmaceutical company that discovers, develops, and commercializes pharmaceutical products for the treatment of serious medical conditions. We currently have one marketed product: ARCALYST<sup>®</sup> (rilonacept) Injection for Subcutaneous Use is now available for 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 also have four clinical development programs, including two late-stage clinical programs. The late stage programs are aflibercept (VEGF Trap), which is being developed in oncology in collaboration with the sanofi-aventis Group and VEGF Trap-Eye, which is being developed in eye diseases using intraocular delivery in collaboration with Bayer HealthCare LLC. ARCALYST<sup>™</sup> (rilonacept; also known as IL-1 Trap) is also in a Phase 2 safety and efficacy trial for the prevention of gout flares induced by the initiation of uric acid-lowering drug therapy used to control gout. Our fourth clinical development program is REGN88, an antibody to the Interleukin-6 receptor (IL-6R) that is being developed with sanofi-aventis. REGN88 entered clinical development in patients with rheumatoid arthritis in the fourth quarter of 2007.

We expect that our next generation of product candidates will be based on our proprietary technologies for developing human monoclonal antibodies. Our antibody program is being conducted in collaboration with sanofi-aventis. Our preclinical research programs are in the areas of oncology and angiogenesis, ophthalmology, metabolic and related diseases, muscle diseases and disorders, inflammation and immune diseases, bone and cartilage, pain, and cardiovascular diseases. Developing and commercializing new medicines entails significant risk and expense. Since inception we have not generated any sales or profits from the commercialization of any of our product candidates.

Our core business strategy is to maintain a strong foundation in basic scientific research and discovery-enabling technology and combine that foundation with our manufacturing and clinical development capabilities to build a successful, integrated biopharmaceutical company. We believe that our ability to develop product candidates is enhanced by the application of our

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technology platforms. Our discovery platforms are designed to identify specific genes of therapeutic interest for a particular disease or cell type and validate targets through high-throughput production of mammalian models. Our human monoclonal antibody technology (*VelocImmune*<sup>®</sup>) and cell line expression technologies may then be utilized to design and produce new product candidates directed against the disease target. Based on the *VelocImmune* platform which we believe, in conjunction with our other proprietary technologies, can accelerate the development of fully human monoclonal antibodies, we moved our first antibody product candidate (REGN88) into clinical trials in 2007. We plan to advance two new antibody product candidates into clinical development in 2008 and an additional two to three antibody product candidates each year thereafter beginning in 2009. We continue to invest in the development of enabling technologies to assist in our efforts to identify, develop, and commercialize new product candidates.

### **ARCALYST<sup>™</sup> (rilonacept) – Inflammatory Diseases:**

ARCALYST<sup>™</sup> (rilonacept; also known as IL-1 Trap) is a protein-based product designed to bind the interleukin-1 (called IL-1) cytokine and prevent its interaction with cell surface receptors. In February 2008, we announced that we had received approval from the U.S. Food and Drug Administration (FDA) for ARCALYST<sup>™</sup> Injection for Subcutaneous Use 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. In July 2007, ARCALYST<sup>™</sup> for the treatment of CAPS received Orphan Drug designation in the European Union.

CAPS represents a group of rare inherited auto-inflammatory conditions. In addition to FCAS and MWS, CAPS includes Neonatal Onset Multisystem Inflammatory Disease (NOMID). ARCALYST<sup>™</sup> has not been studied for the treatment of NOMID. The syndromes included in CAPS are characterized by spontaneous, systemic inflammation and are termed auto-inflammatory disorders. A novel feature of these conditions (particularly FCAS and MWS) is that exposure to mild degrees of cold temperature can provoke a major inflammatory episode that occurs within hours. CAPS is caused by a range of mutations in the gene NLRP3 (formerly known as *CIAS1*) which encodes a protein named cryopyrin.

We are also evaluating ARCALYST<sup>™</sup> in a number of diseases and disorders where IL-1 may play an important role. We have initiated a Phase 2 safety and efficacy trial of ARCALYST<sup>™</sup> in the prevention of gout flares induced by the initiation of uric acid-lowering drug therapy used to control gout. We previously reported positive results from an exploratory proof of concept study of ARCALYST<sup>™</sup> in ten patients with chronic active gout. In those patients, treatment with ARCALYST<sup>™</sup> demonstrated a statistically significant reduction in patient pain scores in the single-blind, placebo-controlled study. Mean patients' pain scores, the key symptom measure in persistent gout, were reduced 41% ( $p=0.025$ ) during the first two weeks of active treatment and reduced 56% ( $p<0.004$ ) after six weeks of active treatment. In this study, in which safety was the primary endpoint measure, treatment with ARCALYST<sup>™</sup> was generally well-tolerated. We are also evaluating the potential use of ARCALYST<sup>™</sup> in other indications in which IL-1 may play a role.

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

Under the collaboration agreement, Novartis has the right to elect to collaborate in the development and commercialization of a second generation IL-1 Trap following completion of its Phase 2 development, should we decide to clinically develop such a second generation product candidate. Novartis does not have any rights or options with respect to ARCALYST™ (rilonacept).

### Late-Stage Clinical Programs:

Below is a summary of the status of our late-stage clinical candidates:

#### **1. Aflibercept (VEGF Trap) – Oncology**

Aflibercept is a protein-based product candidate designed to bind all forms of Vascular Endothelial Growth Factor-A (called VEGF-A, also known as Vascular Permeability Factor or VPF) and the related Placental Growth Factor (called PlGF), and prevent their interaction with cell surface receptors. VEGF-A (and to a less validated degree, PlGF) is required for the growth of new blood vessels that are needed for tumors to grow and is a potent regulator of vascular permeability and leakage.

Aflibercept is being developed in cancer indications in collaboration with sanofi-aventis. We and sanofi-aventis began four Phase 3 trials of aflibercept in the second half of 2007. One trial is evaluating aflibercept as a 1<sup>st</sup> line treatment for metastatic androgen independent prostate cancer in combination with docetaxel/prednisone. A second trial is evaluating aflibercept as a 2<sup>nd</sup> line treatment for metastatic non-small cell lung cancer in combination with docetaxel. The third Phase 3 trial is evaluating aflibercept as a 1<sup>st</sup> line treatment for metastatic pancreatic cancer in combination with gemcitabine. The fourth Phase 3 trial is evaluating aflibercept as a 2<sup>nd</sup> line treatment for metastatic colorectal cancer in combination with FOLFIRI (Folinic Acid (leucovorin), 5-fluorouracil, and irinotecan). In all of these trials, aflibercept is being combined with the current standard of chemotherapy care for the stated development stage of the cancer type.

The collaboration is conducting a number of other trials in the global development program for aflibercept. Five safety and tolerability studies of aflibercept in combination with standard chemotherapy regimens are continuing in a variety of cancer types to support the Phase 3 clinical program. Sanofi-aventis has also expanded the development program to Japan, where they are conducting a Phase 1 safety and tolerability study in combination with another investigational agent in patients with advanced solid malignancies.



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The collaboration is also conducting Phase 2 single-agent studies of aflibercept in advanced ovarian cancer (AOC), non-small cell lung adenocarcinoma (NSCLA), and AOC patients with symptomatic malignant ascites (SMA). We expect to report results from the AOC trial in the second quarter of 2008 and the NSCLA trial by the end of the year. The SMA trial is approximately 50% enrolled and continues to enroll patients. In 2004, the FDA granted Fast Track designation to aflibercept for the treatment of SMA.

In addition, more than 13 studies are currently underway or scheduled to begin that are being conducted in conjunction with the National Cancer Institute (NCI) Cancer Therapy Evaluation Program (CTEP) evaluating aflibercept as a single agent or in combination with chemotherapy regimens in a variety of cancer indications.

The first registration submission to a regulatory agency for aflibercept is possible during 2008, potentially as third line treatment as a single agent in advanced ovarian cancer (AOC) or in AOC patients with SMA. However, in order for our ongoing Phase 2 study in AOC to be sufficient to support such a submission, we believe that the final unblinded results of the study would have to demonstrate a more robust response rate than that reported in the interim analysis of blinded data from the study presented in June 2007 at the annual meeting of the American Society of Clinical Oncology (ASCO).

Cancer is a heterogeneous set of diseases and one of the leading causes of death in the developed world. A mutation in any one of dozens of normal genes can eventually result in a cell becoming cancerous; however, a common feature of cancer cells is that they need to obtain nutrients and remove waste products, just as normal cells do. The vascular system normally supplies nutrients to and removes waste from normal tissues. Cancer cells can use the vascular system either by taking over preexisting blood vessels or by promoting the growth of new blood vessels (a process known as angiogenesis). Vascular Endothelial Growth Factor (VEGF) is secreted by many tumors to stimulate the growth of new blood vessels to supply nutrients and oxygen to the tumor. VEGF blockers have been shown to inhibit new vessel growth, and, in some cases, can cause regression of existing tumor vasculature. Countering the effects of VEGF, thereby blocking the blood supply to tumors, has been shown in clinical trials to have therapeutic benefits. This approach of inhibiting angiogenesis as a mechanism of action for an oncology medicine was validated in February 2004, when the FDA approved Genentech, Inc.'s VEGF inhibitor, Avastin®. Avastin® (a trademark of Genentech, Inc.) is an antibody product designed to inhibit VEGF and interfere with the blood supply to tumors.

### **Aflibercept Collaboration with the sanofi-aventis Group**

In September 2003, we entered into a collaboration agreement with Aventis Pharmaceuticals, Inc. (predecessor to sanofi-aventis U.S.) to collaborate on the development and commercialization of aflibercept in all countries other than Japan, where we retained the exclusive right to develop and commercialize aflibercept. In January 2005, we and sanofi-aventis amended the collaboration agreement to exclude, from the scope of the collaboration, the development and commercialization of aflibercept for intraocular delivery to the eye. In December 2005, we and sanofi-aventis amended our collaboration agreement to expand the territory in which the companies are collaborating on the development of aflibercept to include

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Japan. Under the collaboration agreement, as amended, we and sanofi-aventis will share co-promotion rights and profits on sales, if any, of aflibercept 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 aflibercept, subject to certain potential adjustments. We may also receive up to \$400.0 million in milestone payments upon receipt of specified marketing approvals. This total includes up to \$360.0 million in milestone payments related to receipt of marketing approvals for up to eight aflibercept oncology and other indications in the United States or the European Union. Another \$40.0 million of milestone payments relate to receipt of marketing approvals for up to five oncology indications in Japan.

Under the aflibercept collaboration agreement, as amended, agreed upon worldwide development expenses incurred by both companies during the term of the agreement will be funded by sanofi-aventis. If the collaboration becomes profitable, we will be obligated to reimburse sanofi-aventis for 50% of aflibercept 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.

### **2. VEGF Trap – Eye Diseases**

VEGF Trap-Eye is a form of the VEGF Trap that has been purified and formulated with excipients and at concentrations suitable for direct injection into the eye. We and Bayer HealthCare are currently testing VEGF Trap-Eye in a Phase 3 program in patients with the neovascular form of Age-related Macular Degeneration (wet AMD). The first Phase 3 trial in wet AMD, known as VIEW 1 (VEGF Trap: Investigation of Efficacy and Safety in Wet age-related macular degeneration), is comparing VEGF Trap-Eye and ranibizumab (Lucentis<sup>®</sup>, a registered trademark of Genentech, Inc.), an anti-angiogenic agent approved for use in wet AMD, and is being conducted in North America. This Phase 3 trial is evaluating dosing intervals of four and eight weeks for VEGF Trap-Eye compared with ranibizumab dosed according to its label every four weeks. Bayer HealthCare is initiating a second Phase 3 trial in wet AMD that will be conducted primarily in the European Union and other parts of the world outside the U.S.

In April 2008, we and Bayer HealthCare announced the 32-week endpoint results of a Phase 2 study evaluating VEGF Trap-Eye in wet AMD, which were presented at the 2008 Association for Research in Vision and Ophthalmology (ARVO) meeting in Fort Lauderdale, Florida. The analysis showed that VEGF Trap-Eye dosed on a PRN (as-needed) dosing schedule maintained the statistically significant gain in visual acuity achieved after an initial, 12-week, fixed-dosing phase.

Study results showed that across all dose groups in the study population the 6.6 mean letter gain in visual acuity achieved versus baseline at the week 16 evaluation visit, following 12 weeks of fixed dosing, was maintained out to week 32 (a 6.7 mean letter gain versus baseline;  $p < 0.0001$ ) using a PRN dosing schedule (where dosing frequency was determined by the physician's assessment of pre-specified criteria). The decrease in retinal thickness, an anatomical measure of treatment effect, achieved with a fixed-dose schedule was also maintained for all dose groups combined at week 32 (a 137 micron mean decrease versus baseline,  $p < 0.0001$ ).

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In this double-masked, prospective, randomized, multi-center Phase 2 trial, 157 patients were randomized to five dose groups and treated with VEGF Trap-Eye in one eye. Two groups initially received monthly doses of 0.5 or 2.0 milligrams (mg) of VEGF Trap-Eye for 12 weeks and three groups received quarterly doses of 0.5, 2.0, or 4.0 mg of VEGF Trap-Eye (at baseline and week 12). Following the initial 12-week fixed-dose phase of the trial, patients continued to receive therapy at the same dose on a PRN dosing schedule based upon the physician assessment of the need for re-treatment in accordance with pre-specified criteria. Patients were monitored for safety, retinal thickness, and visual acuity. These data represent the week 32 analysis from the 52-week study, which is continuing to follow patients.

Patients receiving monthly doses of VEGF Trap-Eye, either 0.5 or 2.0 mg, for 12 weeks followed by PRN dosing thereafter achieved mean improvements in visual acuity of 8.0 ( $p < 0.01$  versus baseline) and 10.1 letters ( $p < 0.0001$  versus baseline), respectively, and mean decreases in retinal thickness of 141 ( $p < 0.0001$  versus baseline) and 162 microns ( $p < 0.0001$  versus baseline) at week 32, respectively. While PRN dosing also maintained the improvements in retinal thickness and visual acuity achieved versus baseline following a fixed dosing regimen utilizing quarterly dosing at baseline and week 12, the results achieved with a quarterly fixed dosing regimen were generally not as robust as obtained with initial fixed monthly dosing.

VEGF Trap-Eye was generally safe and well-tolerated and there were no reported drug-related serious adverse events. There was one reported case of culture-negative endophthalmitis/uveitis in the study eye, which was deemed not to be drug-related. The most common adverse events were those typically associated with intravitreal injections.

After the last fixed-dose administration at week 12, patients from all dose groups combined required, on average, only one additional injection over the following 20 weeks to maintain the visual acuity gain established during the fixed-dosing period. Notably, 55% of the patients who received 2.0 mg monthly for 12 weeks did not require any additional treatment throughout the next 20-week PRN dosing period. Moreover, 97% of the patients who received 2.0 mg monthly for 12 weeks did not require re-dosing at the week 16 evaluation visit, indicating that an 8-week dosing schedule may be feasible.

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

Wet AMD and diabetic retinopathy (DR) are two of the leading causes of adult blindness in the developed world. In both conditions, severe visual loss is caused by a combination of retinal edema and neovascular proliferation.

### **Collaboration with Bayer HealthCare**

In October 2006, we entered into a collaboration agreement with Bayer HealthCare for the global development and commercialization outside the United States of VEGF Trap-Eye. Under

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the agreement, we and Bayer HealthCare will collaborate on, and share the costs of, the development of VEGF Trap-Eye through an integrated global plan that encompasses wet AMD, diabetic eye diseases, and other diseases and disorders. Bayer HealthCare will market VEGF Trap-Eye outside the United States, where the companies will share equally in profits from any future sales of VEGF Trap-Eye. If VEGF Trap-Eye is granted marketing authorization 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. Within the United States, we retain exclusive commercialization rights to VEGF Trap-Eye and are entitled to all profits from any such sales. We received an up-front payment of \$75.0 million from Bayer HealthCare. In 2007, we received a \$20.0 million milestone payment from Bayer HealthCare following dosing of the first patient in the Phase 3 study of VEGF Trap-Eye in wet AMD, and can earn up to \$90.0 million in additional development and regulatory milestones related to the development of VEGF Trap-Eye and marketing approvals in major market countries outside the United States. We can also earn up to \$135.0 million in sales milestones if total annual sales of VEGF Trap-Eye outside the United States achieve certain specified levels starting at \$200.0 million.

### **Antibody Research Technologies and Development Program:**

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

Regeneron scientists have developed two different technologies to design protein therapeutics to block the action of specific secreted proteins. The first technology, termed the “Trap” technology, was used to generate our first approved product, ARCALYST™ (rilonacept) for the treatment of CAPS, and our current clinical pipeline, including aflibercept, VEGF Trap-Eye, and ARCALYST™ in other indications. 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.

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

### ***VelocImmune*® (Human Monoclonal Antibodies)**

We have developed a novel mouse technology platform, called *VelocImmune*, for producing fully human monoclonal antibodies. The *VelocImmune* mouse platform was generated by

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

### **Antibody Collaboration with sanofi-aventis**

In November 2007, we and sanofi-aventis entered into a global, strategic collaboration to discover, develop, and commercialize fully human monoclonal antibodies. The first therapeutic antibody to enter clinical development under the collaboration, REGN88, is an antibody to the Interleukin-6 receptor (IL-6R), which has started clinical trials in rheumatoid arthritis. The second is expected to be an antibody to Delta-like ligand-4 (Dll4), which is currently scheduled to commence clinical development in mid-2008. The collaboration is governed by a Discovery and Preclinical Development Agreement and a License and Collaboration Agreement. We received a non-refundable, up-front payment of \$85.0 million from sanofi-aventis under the discovery agreement. In addition, sanofi-aventis will fund up to \$475.0 million of our research for identifying and validating potential drug discovery targets and developing fully human monoclonal antibodies against these targets through December 31, 2012. Sanofi-aventis also has an option to extend the discovery program for up to an additional three years for further antibody development and preclinical activities.

For each drug candidate identified under the discovery agreement, sanofi-aventis has the option to license rights to the candidate under the license agreement. If it elects to do so, sanofi-aventis will co-develop the drug candidate with us through product approval. Development costs will be shared between the companies, with sanofi-aventis funding drug candidate development costs up front. We are generally responsible for reimbursing sanofi-aventis for half of the total development costs for all collaboration products from our share of profits from commercialization of collaboration products to the extent they are sufficient for this purpose. Sanofi-aventis 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-aventis)/35% (us) and ending at 55% (sanofi-aventis)/45% (us), and will share losses outside the United States at 55% (sanofi-aventis)/45% (us). In addition to profit sharing, we are entitled to receive up to \$250.0 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.

### **License Agreement with AstraZeneca**

In February 2007, we entered into a non-exclusive license agreement with AstraZeneca UK Limited that allows AstraZeneca to utilize our *VelocImmune* technology in its internal research

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programs to discover human monoclonal antibodies. Under the terms of the agreement, AstraZeneca made two \$20.0 million annual, non-refundable payments to us, one in February 2007, and the other in February 2008. AstraZeneca is required to make up to four remaining additional annual payments of \$20.0 million, subject to its ability to terminate the agreement after making two such additional payments or earlier if the technology does not meet minimum performance criteria. We are entitled to receive a mid-single-digit royalty on any future sales of antibody products discovered by AstraZeneca using our *VelocImmune* technology.

### **License Agreement with Astellas**

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

### **VelociGene® and VelociMouse™ (Target Validation)**

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

The *VelociMouse* technology also allows for the direct and immediate generation of genetically altered mice from 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, Regeneron's *VelociMice* are suitable for direct phenotyping or other studies.

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

In September 2006, we were awarded a five-year grant from the National Institutes of Health (NIH) as part of the NIH's Knockout Mouse Project. The goal of the Knockout Mouse Project is to build a comprehensive and broadly available resource of knockout mice to accelerate the understanding of gene function and human diseases. We use our *VelociGene* technology to take aim at 3,500 of the most difficult genes to target and which are not currently the focus of other large-scale knockout mouse programs. We also agreed to grant a limited license to a consortium

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of research institutions, the other major participants in the Knockout Mouse Project, to use components of our *VelociGene* technology in the Knockout Mouse Project. We are generating a collection of targeting vectors and targeted mouse ES cells which can be used to produce knockout mice. These materials will be made widely available to academic researchers without charge. We will receive a fee for each targeted ES cell line or targeting construct made by us or the research consortium and transferred to commercial entities.

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

### **Cell Line Expression Technologies**

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

### **General**

Developing and commercializing new medicines entails significant risk and expense. Before revenues from the commercialization of product candidates can be realized, we (or our collaborators) must overcome a number of hurdles which include successfully completing research and development and obtaining regulatory approval from the FDA and regulatory authorities in other countries. In addition, the biotechnology and pharmaceutical industries are rapidly evolving and highly competitive, and new developments may render our products and technologies uncompetitive or obsolete.

From inception on January 8, 1988 through March 31, 2008, we have not recognized any sales or generated any profits from the commercialization of any of our product candidates, and had a cumulative loss of \$804.8 million. As described above, in February 2008, we received FDA approval for ARCALYST™ (riloncept) for the treatment of CAPS. These rare diseases affect a very small group of people. As a result, we can not predict whether the commercialization of ARCALYST™ in CAPS will result in a significant net cash benefit to us. In the absence of significant revenues from the commercialization of our product candidates or other sources, the amount, timing, nature, and source of which cannot be predicted, our losses will continue as we conduct our research and development activities. We expect to incur substantial losses over the next several years as we continue the clinical development of VEGF Trap-Eye and ARCALYST™ in other indications; advance new product candidates into clinical development from our existing research programs utilizing our technology for designing fully human monoclonal antibodies; continue our research and development programs; and commercialize product candidates that receive regulatory approval, if any. Also, our activities may expand over

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time and require additional resources, and we expect our operating losses to be substantial over at least the next several years. Our losses may fluctuate from quarter to quarter and will depend on, among other factors, the progress of our research and development efforts, the timing of certain expenses, and the amount and timing of payments that we receive from collaborators.

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 2008 and plans over the next 12 months are as follows:

<u>Clinical Program</u>	<u>2008 Events to Date</u>	<u>2008-9 Plans</u>
ARCALYST™ (rilonacept; also known as IL-1 Trap)	<ul style="list-style-type: none"><li>Received FDA approval for CAPS</li><li>Launched ARCALYST™ commercially in CAPS</li></ul>	<ul style="list-style-type: none"><li>Evaluate ARCALYST™ in gout and certain other disease indications in which IL-1 may play an important role</li></ul>
Aflibercept (VEGF Trap – Oncology)		<ul style="list-style-type: none"><li>Sanofi-aventis to initiate additional studies of aflibercept in combination with standard chemotherapy regimens</li><li>Report final data from Phase 2 single-agent trials in advanced ovarian cancer and in non-small cell lung adenocarcinoma</li><li>Complete enrollment of Phase 2 single-agent study in symptomatic malignant ascites (SMA)</li><li>NCI/CTEP to begin to report data from trials</li><li>NCI/CTEP to initiate additional exploratory safety and efficacy studies</li></ul>
VEGF Trap-Eye (intravitreal injection)	<ul style="list-style-type: none"><li>Presented positive extended follow-up data through 32 weeks from the Phase 2 trial in wet AMD</li></ul>	<ul style="list-style-type: none"><li>Initiate second Phase 3 trial in wet AMD in the European Union and certain other ex-U.S. countries</li><li>Explore additional eye disease indications</li></ul>
Antibodies	<ul style="list-style-type: none"><li>Finalized preparations for initiation of clinical program for the Dll4 antibody</li></ul>	<ul style="list-style-type: none"><li>Initiate Phase 1 trial for the Dll4 antibody in oncology</li><li>Report data from Phase 1 trial of REGN88 in rheumatoid arthritis</li><li>Advance a third antibody candidate into clinical development</li></ul>



## **ARCALYST™ (riloncept) Product Revenue and Inventory**

### **Product Revenue**

In late March 2008, ARCALYST™ became available for prescription in the United States for the treatment of CAPS and we made our first shipments of ARCALYST™ to our distributors. We will recognize revenue from product sales in accordance with Staff Accounting Bulletin No. 104, *Revenue Recognition* (SAB 104). Revenue from product sales is recognized when persuasive evidence of an arrangement exists, title to product and associated risk of loss has passed to the customer, the price is fixed or determinable, collection from the customer is reasonably assured and we have no further performance obligations. When recognized, revenues from product sales will be recorded net of applicable provisions for prompt pay discounts, product returns, and estimated rebates. We will account for these reductions in accordance with Emerging Issues Task Force Issue No. 01-9, *Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor's Products)* (EITF 01-9), and Statement of Financial Accounting Standards No. (SFAS) 48, *Revenue Recognition When Right of Return Exists*, as applicable.

Since we have no historical return or rebate experience for ARCALYST™, no product sales revenue has been recognized in the first quarter of 2008, and revenue recognition has been fully deferred until the right of return no longer exists and rebates have been processed, or until we can reasonably estimate returns and rebates. At March 31, 2008, deferred revenue related to ARCALYST™ product sales totaled \$0.8 million.

### **Inventory**

We began capitalizing inventory costs associated with commercial supplies of ARCALYST™ subsequent to receipt of marketing approval from the FDA on February 27, 2008. Costs for manufacturing supplies of ARCALYST™ prior to receipt of FDA approval were recognized as research and development expenses in the period incurred; therefore, these costs will not be included in cost of goods sold when those supplies of ARCALYST™ are sold. As a result, in 2008, we anticipate that ARCALYST™ cost of goods sold will be insignificant. At March 31, 2008, inventoried costs related to ARCALYST™ were inconsequential.

## **Results of Operations**

### **Three Months Ended March 31, 2008 and 2007**

#### *Net Loss:*

Regeneron reported a net loss of \$11.6 million, or \$0.15 per share (basic and diluted), for the first quarter of 2008 compared to a net loss of \$29.9 million, or \$0.46 per share (basic and diluted), for the first quarter of 2007. The decrease in the Company's net loss was principally due to revenues earned in the first quarter of 2008 in connection with our antibody collaboration with sanofi-aventis and our VEGF Trap-Eye collaboration with Bayer HealthCare, partly offset by higher research and development expenses.

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### Revenues:

Revenues for the three months ended March 31, 2008 and 2007 consist of the following:

<i>(In millions)</i>	<u>2008</u>	<u>2007</u>
Contract research & development revenue		
Sanofi-aventis	\$ 35.7	\$ 11.8
Bayer HealthCare	9.0	
Other	1.7	1.9
Total contract research & development revenue	<u>46.4</u>	<u>13.7</u>
Technology licensing revenue	10.0	2.1
Total revenue	<u>\$ 56.4</u>	<u>\$ 15.8</u>

We recognize revenue from sanofi-aventis, in connection with our aflibercept and antibody collaborations, in accordance with SAB 104 and FASB Emerging Issue Task Force Issue No. 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables* (EITF 00-21). We earn contract research and development revenue from sanofi-aventis which, as detailed below, consists partly of reimbursement for research and development expenses and partly of the recognition of revenue related to non-refundable, up-front payments of \$105.0 million related to the aflibercept collaboration and \$85.0 million related to the antibody collaboration. Non-refundable, up-front payments are recorded as deferred revenue and recognized over the period over which we are obligated to perform services. We estimate our performance periods based on the specific terms of the collaboration agreements, and adjust the performance periods, if appropriate, based on the applicable facts and circumstances.

<u>Sanofi-aventis Contract Research &amp; Development Revenue</u> <i>(In millions)</i>	<u>Three months ended</u> <u>March 31,</u>	
	<u>2008</u>	<u>2007</u>
Aflibercept:		
Regeneron expense reimbursement	\$ 11.7	\$ 9.6
Recognition of deferred revenue related to up-front payments	2.1	2.2
Total aflibercept	<u>13.8</u>	<u>11.8</u>
Antibody:		
Regeneron expense reimbursement	19.3	
Recognition of deferred revenue related to up-front payments	2.6	
Total antibody	<u>21.9</u>	
Total sanofi-aventis contract research & development revenue	<u>\$ 35.7</u>	<u>\$ 11.8</u>

Sanofi-aventis' reimbursement of Regeneron's aflibercept expenses increased in the first quarter of 2008 compared to the same period in 2007, primarily due to higher costs related to our manufacture of aflibercept clinical supplies and higher clinical development costs. Recognition of deferred revenue related to sanofi-aventis' up-front aflibercept payments decreased in the first quarter of 2008 compared to the same period in 2007 due to an extension of the estimated performance period over which this deferred revenue is being recognized. As of March 31, 2008, \$59.1 million of the original \$105.0 million of up-front payments related to aflibercept was deferred and will be recognized as revenue in future periods.

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In the first quarter of 2008, sanofi-aventis' reimbursement of Regeneron's antibody expenses consisted of \$15.1 million under the collaboration's discovery agreement and \$4.2 million of REGN88 development costs under the license agreement. Recognition of deferred revenue under the antibody collaboration related to sanofi-aventis' \$85.0 million up-front payment. As of March 31, 2008, \$81.5 million of this up-front payment was deferred and will be recognized as revenue in future periods.

In connection with our VEGF Trap-Eye collaboration with Bayer HealthCare, through September 30, 2007, all payments received from Bayer HealthCare, including a \$75.0 million non-refundable, up-front payment, a \$20.0 million milestone payment (which was received in August 2007 and not considered substantive), and cost sharing reimbursements were fully deferred and included in deferred revenue. Effective in the fourth quarter of 2007, we determined the appropriate accounting policy for payments from Bayer HealthCare and commenced recognizing previously deferred payments and cost-sharing of our and Bayer HealthCare's 2007 VEGF Trap-Eye development expenses in our Statement of Operations through a cumulative catch-up. The \$75.0 million non-refundable, up-front license payment and the \$20.0 million milestone payment are being recognized as contract research and development revenue over the related estimated performance period in accordance with SAB 104 and EITF 00-21. In periods when we recognize VEGF Trap-Eye development expenses that we incur under the collaboration, we also recognize, as contract research and development revenue, the portion of those VEGF Trap-Eye development expenses that is reimbursable from Bayer HealthCare. In periods when Bayer HealthCare incurs agreed upon VEGF Trap-Eye development expenses that benefit the collaboration and Regeneron, we also recognize, as additional research and development expense, the portion of Bayer HealthCare's VEGF Trap-Eye development expenses that we are obligated to reimburse. In the first quarter of 2008, we recognized contract research and development revenue of \$9.0 million from Bayer HealthCare, consisting of (i) \$3.3 million related to the \$75.0 million up-front licensing payment and the \$20.0 million milestone payment, and (ii) \$5.7 million related to the portion of our first quarter 2008 VEGF Trap-Eye development expenses that is reimbursable from Bayer HealthCare. As of March 31, 2008, \$75.8 million of the up-front licensing and milestone payments was deferred and will be recognized as revenue in future periods.

Other contract research and development revenue includes \$1.1 million and \$0.7 million, respectively, recognized in the first quarter of 2008 and 2007 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.

In connection with our license agreements with AstraZeneca and Astellas, each of the \$20.0 million annual, non-refundable payments are deferred upon receipt and recognized as revenue ratably over approximately the ensuing year of each agreement. In the first quarter of 2008 and 2007, we recognized \$10.0 million and \$2.1 million, respectively, of technology licensing revenue related to these agreements.

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### Expenses:

Total operating expenses increased to \$72.3 million in the first quarter of 2008 from \$49.4 million in the same period of 2007. Our average headcount increased to 714 in the first quarter of 2008 from 585 in the same period of 2007 primarily to support expanding research and development activities for our development programs, including ARCALYST™ (rilonacept), aflibercept, VEGF Trap-Eye, and monoclonal antibodies (such as REGN88 and the D114 antibody).

Operating expenses in the first quarter of 2008 and 2007 include a total of \$8.3 million and \$6.6 million, respectively, of non-cash compensation expense related to employee stock option and restricted stock awards (Non-cash Compensation Expense), as detailed below:

<u>Expenses</u> <i>(In millions)</i>	<u>For the three months ended March 31, 2008</u>		
	<u>Expenses before inclusion of Non-cash Compensation Expense</u>	<u>Non-cash Compensation Expense</u>	<u>Expenses as Reported</u>
Research and development	\$ 56.4	\$ 4.9	\$ 61.3
Selling, General and administrative	7.6	3.4	11.0
Total operating expenses	<u>\$ 64.0</u>	<u>\$ 8.3</u>	<u>\$ 72.3</u>

<u>Expenses</u> <i>(In millions)</i>	<u>For the three months ended March 31, 2007</u>		
	<u>Expenses before inclusion of Non-cash Compensation Expense</u>	<u>Non-cash Compensation Expense</u>	<u>Expenses as Reported</u>
Research and development	\$ 37.4	\$ 3.8	\$ 41.2
Selling, General and administrative	5.4	2.8	8.2
Total operating expenses	<u>\$ 42.8</u>	<u>\$ 6.6</u>	<u>\$ 49.4</u>

### Research and Development Expenses:

Research and development expenses increased to \$61.3 million in the first quarter of 2008 from \$41.2 million in the same period of 2007. The following table summarizes the major categories of our research and development expenses for the three months ended March 31, 2008 and 2007:

<u>Research and development expenses</u> <i>(In millions)</i>	<u>For the three months ended March 31,</u>		
	<u>2008</u>	<u>2007</u>	<u>Increase (Decrease)</u>
Payroll and benefits (1)	\$ 19.2	\$ 13.7	\$ 5.5
Clinical trial expenses	8.5	5.3	3.2
Clinical manufacturing costs (2)	14.7	10.5	4.2
Research and preclinical development costs	5.5	6.0	(0.5)
Occupancy and other operating costs	6.8	5.7	1.1
Cost-sharing of Bayer HealthCare VEGF Trap-Eye development expenses (3)	6.6		6.6
Total research and development expenses	<u>\$ 61.3</u>	<u>\$ 41.2</u>	<u>\$ 20.1</u>

(1) Includes \$4.2 million and \$3.1 million of Non-cash Compensation Expense for the three months ended March 31, 2008 and 2007, respectively.

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- (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, depreciation, and occupancy costs of our Rensselaer manufacturing facility. Includes \$0.7 million of Non-cash Compensation Expense for both the three months ended March 31, 2008 and 2007.
- (3) Under our collaboration with Bayer HealthCare, in periods when Bayer HealthCare incurs VEGF Trap-Eye development expenses, we also recognize, as additional research and development expense, the portion of their VEGF Trap-Eye development expenses that we are obligated to reimburse. In the fourth quarter of 2007, we commenced recognizing cost-sharing of our and Bayer Healthcare's VEGF Trap-Eye development expenses.

Payroll and benefits increased principally due to the increase in employee headcount, as described above. Clinical trial expenses increased due primarily to higher costs related to our Phase 3 study of VEGF Trap-Eye in wet AMD, which we initiated in the third quarter of 2007, and higher ARCALYST™ costs, primarily related to our Phase 2 gout-induced flares clinical study. These increases were partially offset by lower costs related to our Phase 1 and 2 studies of VEGF Trap-Eye in wet AMD. Clinical manufacturing costs increased due primarily to higher expenses related to aflibercept, VEGF Trap-Eye, and our Dll4 antibody, partially offset by lower costs related to ARCALYST™ and REGN88. Research and preclinical development costs decreased primarily due to lower preclinical costs associated with aflibercept, VEGF Trap-Eye, and REGN88, partially offset by higher costs related to our Dll4 antibody. Occupancy and other operating costs primarily increased in connection with our higher headcount and to support our expanded research and development activities.

We budget our research and development costs by expense category, rather than by project. We also prepare estimates of research and development cost 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 VEGF Trap-Eye development expenses that we are obligated to reimburse. Our estimates of research and development costs for clinical development programs (including ARCALYST™ for the treatment of CAPS prior to receipt of marketing approval from the FDA in February 2008) are shown below:

<b>Project Costs</b> <i>(In millions)</i>	<b>For the three months ended March 31,</b>		
	<b>2008</b>	<b>2007</b>	<b>Increase (Decrease)</b>
ARCALYST™ (rilonacept)	\$ 8.0	\$ 7.7	\$ 0.3
Aflibercept	10.1	7.8	2.3
VEGF Trap-Eye	16.6	5.8	10.8
REGN88	9.3	4.8	4.5
Other research programs & unallocated costs	17.3	15.1	2.2
Total research and development expenses	<u>\$ 61.3</u>	<u>\$ 41.2</u>	<u>\$ 20.1</u>

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: Phase 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 biologics license application (or 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™ (rilonacept), aflibercept, and VEGF Trap-Eye 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 ARCALYST™ and the Development of Our Product Candidates,” “Regulatory and Litigation Risks,” and “Risks Related to Commercialization of Products.” 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 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 will generate material product revenues and net cash inflows. In the first quarter of 2008, we received FDA approval for ARCALYST™ for the treatment of CAPS, a group of rare, inherited auto-inflammatory diseases. These rare diseases affect a very small group of people. As a result, we can not predict whether the commercialization of ARCALYST™ in CAPS will result in a significant net cash benefit to us.

*Selling, General, and Administrative Expenses:*

Selling, general, and administrative expenses increased to \$11.0 million in the first quarter of 2008 from \$8.2 million in the same period of 2007 due in part to costs associated with the launch of ARCALYST™ in March 2008. In addition, during the first quarter of 2008, we incurred (i) higher compensation expense due primarily to increases in selling and administrative headcount to support our expanded research and development activities and ARCALYST™ commercialization activities, (ii) higher recruitment and related costs associated with expanding our headcount, and (iii) higher legal expenses related to general corporate matters.

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### *Other Income and Expense:*

Investment income increased to \$7.3 million in the first quarter of 2008 from \$6.7 million in the comparable quarter of 2007. The increase in investment income resulted primarily from higher balances of cash and marketable securities, due primarily to our receipt from sanofi-aventis of \$312.0 million for the purchase of 12 million shares of our Common Stock in December 2007 and the \$85.0 up-front payment related to the antibody collaboration, partially offset by lower effective interest rates. Interest expense was \$3.0 million in the first quarter of 2008 and 2007. Interest expense is attributable to \$200.0 million of convertible notes issued in October 2001, which mature in October 2008 and bear interest at 5.5% per annum.

### **Accounting for Fair Value of Financial Assets**

#### ***Adoption of Statement of Financial Accounting Standard No. 157***

In September 2006, the Financial Accounting Standards Board issued SFAS 157, *Fair Value Measurements*. SFAS 157 defines fair value, establishes a framework for measuring fair value in accordance with accounting principles generally accepted in the United States, and expands disclosures about fair value measurements. We adopted the provisions of SFAS 157 as of January 1, 2008, for financial instruments. Although the adoption of SFAS 157 did not materially impact our financial condition, results of operations, or cash flows, we are now required to provide additional disclosures as part of our financial statements.

SFAS 157 establishes 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.

We have determined that the provisions of SFAS 157 are applicable to our marketable securities, which totaled \$305.4 million as of March 31, 2008, and consisted of obligations of the U.S. government and its agencies, investment grade debt securities issued by corporations, governments and financial institutions, asset-backed securities, and commercial paper. All of our marketable securities are considered to be "available for sale," as defined by SFAS 115, *Accounting for Certain Investments in Debt and Equity Securities*. At March 31, 2008, less than 3% of our marketable securities represented Level 3 assets, and our other marketable securities represented Level 2 assets. During the quarter ended March 31, 2008, there were no purchases, sales, or maturities of Level 3 marketable securities, and no transfers of marketable securities between the Level 2 and Level 3 classifications. We held no Level 1 marketable securities during the quarter.

Our methods for valuing our marketable securities are described in Note 5 to our condensed financial statements included in this quarterly report on Form 10-Q. With respect to valuations received from our investment advisors for pricing our Level 2 marketable securities, we review our investment advisors' policies and procedures for valuation. For valuations that we determine

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for our Level 3 marketable securities, we regularly monitor these securities and adjust their valuations as deemed appropriate based on the facts and circumstances.

### **Liquidity and Capital Resources**

Since our inception in 1988, we have financed our operations primarily through offerings of our equity securities, a private placement of convertible debt, revenue earned under our past and present research and development and contract manufacturing agreements, including our agreements with sanofi-aventis and Bayer HealthCare, and investment income.

#### ***Three months ended March 31, 2008 and 2007***

At March 31, 2008, we had \$827.9 million in cash, cash equivalents, restricted cash, and marketable securities compared with \$846.3 million at December 31, 2007. In February 2008, we received a \$20.0 million annual, non-refundable payment in connection with our non-exclusive license agreement with AstraZeneca.

#### ***Cash (Used in) Provided by Operations:***

Net cash used in operations was \$17.9 million in the first quarter of 2008 compared to \$9.2 million in the first quarter of 2007. Our net losses of \$11.6 million in the first quarter of 2008 and \$29.9 million in the first quarter of 2007 included \$8.3 million and \$6.6 million, respectively, of Non-cash Compensation Expense.

At March 31, 2008, accounts receivable increased by \$14.6 million, compared to end-of-year 2007, primarily due to higher receivable balances related to our collaborations with sanofi-aventis. Accounts payable, accrued expenses, and other liabilities decreased by \$7.6 million at March 31, 2008, compared to end-of-year 2007, due primarily to reductions in accrued payroll costs and the amount of the cost-sharing payment due to Bayer HealthCare in connection with the companies' VEGF Trap-Eye collaboration.

At March 31, 2007, accounts receivable balances increased by \$26.1 million, compared to end-of-year 2006, primarily due to a \$20.0 million non-refundable, up-front payment which was receivable in connection with our non-exclusive license agreement with Astellas. Our deferred revenue balances at March 31, 2007 increased by \$37.7 million, compared to end-of-year 2006, primarily due to the initial \$20.0 million non-refundable, up-front payments received or receivable from AstraZeneca and Astellas as of March 31, 2007. These initial up-front payments have been recognized as revenue ratably over approximately the ensuing year of each non-exclusive license agreement.

#### ***Cash Used in Investing Activities:***

Net cash provided by investing activities was \$37.9 million in the first quarter of 2008 compared to net cash used in investing activities of \$74.1 million in the same period of 2007, due primarily to a decrease in purchases of marketable securities net of sales or maturities. In the first quarter of 2008, sales or maturities exceeded purchases of marketable securities by \$41.0



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million, whereas in the first quarter of 2007, purchases of marketable securities exceeded sales or maturities by \$72.9 million.

### *Cash Provided by Financing Activities:*

Cash provided by financing activities decreased slightly to \$1.9 million in the first quarter of 2008 from \$2.0 million in the same period in 2007 due to a decrease in issuances of Common Stock in connection with exercises of employee stock options.

### *Capital Expenditures:*

Our additions to property, plant, and equipment totaled \$2.8 million and \$1.0 million for the first three months of 2008 and 2007, respectively. During the remainder of 2008, we expect to incur approximately \$55 to \$65 million in capital expenditures primarily in connection with expanding our manufacturing capacity at our Rensselaer, New York facilities and tenant improvements and related costs in connection with our new Tarrytown operating lease. We expect that approximately \$30 million of projected 2008 Tarrytown tenant improvement costs will be reimbursed by our landlord in connection with our new operating lease. We currently anticipate that other 2008 capital expenditures will be funded from our existing capital resources.

### *Convertible Debt:*

In 2001, we issued \$200.0 million aggregate principal amount of convertible senior subordinated notes, which bear interest at 5.5% per annum, payable semi-annually, and mature in October 2008. The notes are convertible into shares of our Common Stock at a conversion price of approximately \$30.25 per share, subject to adjustment in certain circumstances. If the price per share of our Common Stock is above \$30.25 at maturity, we would expect the notes to convert into shares of Common Stock. Otherwise, we will be required to repay the \$200.0 million aggregate principal amount of the notes from our existing capital resources or refinance the notes prior to maturity; however, we can provide no assurance that we will be able to successfully arrange such refinancing.

### *Funding Requirements:*

We expect to continue to incur substantial funding requirements primarily for research and development activities (including preclinical and clinical testing). Before taking into account reimbursements from collaborators and potential repayment of our convertible debt (as described above), and exclusive of product revenues and costs in connection with ARCALYST™ (rilonacept) for the treatment of CAPS, we currently anticipate that approximately 55-65% of our expenditures for 2008 will be directed toward the preclinical and clinical development of product candidates, including ARCALYST™ in other indications, aflibercept, VEGF Trap-Eye, and monoclonal antibodies (including REGN88 and the Dll4 antibody); approximately 15-20% of our expenditures for 2008 will be applied to our basic research and early preclinical activities, and the remainder of our expenditures for 2008 will be used for the continued development of our novel technology platforms, capital expenditures, and general corporate purposes.

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We currently anticipate that in 2008 the commercialization of ARCALYST™ (riloncept) for the treatment of CAPS will not materially enhance or otherwise materially impact the Company's cash flows.

The amount we need to fund our operations will depend on various factors, including the status of competitive products, sales of ARCALYST™, the success of our research and development programs, the potential future need to expand our professional and support staff and facilities, the status of patents and other intellectual property rights, the delay or failure of a clinical trial of any of our potential drug candidates, and the continuation, extent, and success of our collaborations with sanofi-aventis 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. In the future, if we are able to successfully develop, market, and sell certain of our product candidates, we may be required to pay royalties or otherwise share the profits generated on such sales in connection with our collaboration and licensing agreements.

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

We believe that our existing capital resources, including funding we are entitled to receive under our collaboration and licensing agreements, will enable us to meet operating needs through at least 2012. However, this is a forward-looking statement based on our current operating plan, and there may be a change in projected revenues or expenses that would lead to our capital being consumed significantly before such time. If there is insufficient capital to fund all of our planned operations and activities, we believe we would prioritize available capital to fund the commercialization of ARCALYST™ and the cost of preclinical and clinical development of our product candidates. Other than letters of credit totaling \$1.7 million, including a \$1.6 million letter of credit issued to our landlord in connection with our new operating lease for facilities in Tarrytown, New York, we have no off-balance sheet arrangements. In addition, we do not guarantee the obligations of any other entity. As of March 31, 2008, we had no established banking arrangements through which we could obtain short-term financing or a line of credit. In the event we need additional financing for the operation of our business, we will consider collaborative arrangements and additional public or private financing, including additional equity financing. Factors influencing the availability of additional financing include our progress in product development, investor perception of our prospects, and the general condition of the financial markets. We may not be able to secure the necessary funding through new collaborative arrangements or additional public or private offerings. If we cannot raise adequate funds to satisfy our capital requirements, we may have to delay, scale-back, or eliminate certain of our research and development activities or future operations. This could materially harm our business.

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

In November 2007, the Emerging Issues Task Force issued Statement No. 07-1, *Accounting for Collaborative Arrangements* (“EITF 07-1”). EITF 07-01 defines collaborative arrangements and establishes reporting requirements for transactions between participants in a collaborative arrangement and between participants in the arrangement and third parties. EITF 07-1 also establishes the appropriate income statement presentation and classification for joint operating activities and payments between participants, as well as the sufficiency of the disclosures related to these arrangements. EITF 07-1 is effective for fiscal years beginning after December 15, 2008, and will be applied retrospectively as a change in accounting principle for collaborative arrangements existing at the effective date. We are required to adopt EITF 07-1 for the fiscal year beginning January 1, 2009. Our management does not anticipate that the adoption of EITF 07-1 will have a material impact on our financial statements.

### **Item 3. Quantitative and Qualitative Disclosure About Market Risk**

#### *Interest Rate Risk:*

Our earnings and cash flows are subject to fluctuations due to changes in interest rates primarily from our investment of available cash balances in investment grade corporate, asset-backed, and U.S. government securities. We do not believe we are materially exposed to changes in interest rates. Under our current policies, we do not use interest rate derivative instruments to manage exposure to interest rate changes. We estimated that a one percent unfavorable change in interest rates would result in approximately a \$1.8 million decrease in the fair value of our investment portfolio at both March 31, 2008 and 2007.

#### *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. In the second half of 2007, we recognized a \$5.9 million charge related to marketable securities which we considered to be other than temporarily impaired in value.

### **Item 4. Controls and Procedures**

Our management, with the participation of our chief executive officer and chief financial officer, conducted an evaluation of the effectiveness of our 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, as amended (the “Exchange Act”)), as of the end of the period covered by this report. 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 us in the reports that we file or submit under the Exchange Act is recorded, processed, summarized, and reported within the time periods specified in applicable rules and forms of the Securities and Exchange Commission, and

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is accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate to allow timely decisions regarding required disclosure.

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 March 31, 2008 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

## **PART II. OTHER INFORMATION**

### **Item 1. Legal Proceedings**

For a description of a dispute between us and Collectis Inc. regarding the scope of our license agreement with them with respect to a family of patents related to homologous recombination, see Item 1A “Risk Factors” – “Risks Related to Intellectual Property”; “*We may be restricted in our development and/or commercialization activities by, and could be subject to damage awards if we are found to have infringed, third party patents or other proprietary rights.*”

### **Item 1A. Risk Factors**

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

#### **Risks Related to Our Financial Results and Need for Additional Financing**

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

From inception on January 8, 1988 through March 31, 2008, we had a cumulative loss of \$804.8 million. 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 or other sources, the amount, timing, nature or source of which cannot be predicted, our losses will continue as we conduct our research and development activities.

***We 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. We believe our existing capital

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resources, including funding we are entitled to receive under our collaboration agreements, will enable us to meet operating needs through at least 2012; however, one or more of our collaboration agreements may terminate, our projected revenue may decrease, or our expenses may increase and that would lead to our capital being consumed significantly before such time. We may require additional financing in the future and we may not be able to raise such additional funds. If we are able to obtain additional financing through the sale of equity or convertible debt securities, such sales may be dilutive to our shareholders. Debt financing arrangements may require us to pledge certain assets or enter into covenants that would restrict our business activities or our ability to incur further indebtedness and may contain other terms that are not favorable to our shareholders. If we are unable to raise sufficient funds to complete the development of our product candidates, we may face delay, reduction or elimination of our research and development programs or preclinical or clinical trials, in which case our business, financial condition or results of operations may be materially harmed.

***We have a significant amount of debt that is scheduled to mature in 2008.***

We have \$200.0 million of convertible debt that, unless converted to shares of our Common Stock, will mature in October 2008. We could be required to use a significant portion of our cash to repay the principal amount of our debt.

### **Risks Related to ARCALYST™ (rilonacept) and the Development of Our Product Candidates**

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

Only a small minority of all research and development programs ultimately result in commercially successful drugs. Even if clinical trials demonstrate safety and effectiveness of any of our product candidates for a specific disease and the necessary regulatory approvals are obtained, the commercial success of any of our product candidates will depend upon their acceptance by patients, the medical community, and third-party payers and on our partners' ability to successfully manufacture and commercialize our product candidates. Our product candidates are delivered either by intravenous infusion or by intravitreal or subcutaneous injections, which are generally less well received by patients than tablet or capsule delivery. If our products are not successfully commercialized, we will not be able to recover the significant investment we have made in developing such products and our business would be severely harmed.

We are studying aflibercept, VEGF Trap-Eye, and ARCALYST™, in a wide variety of indications. We are studying aflibercept in a variety of cancer settings, VEGF Trap-Eye in different eye diseases and ophthalmologic indications, and ARCALYST™ in a variety of systemic inflammatory disorders. Many of these current trials are exploratory studies designed to identify what diseases and uses, if any, are best suited for our product candidates. It is likely that our product candidates will not demonstrate the requisite efficacy and/or safety profile to support continued development for most of the indications that are being, or are planned to be, studied. In fact, our product candidates may not demonstrate the requisite efficacy and safety profile to support the continued development for any of the indications or uses.

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

We must conduct extensive testing of our product candidates before we can obtain regulatory approval to market and sell them. We need to conduct both preclinical animal testing and human clinical trials. Conducting these trials is a lengthy, time-consuming, and expensive process. These tests and trials may not achieve favorable results for many reasons, including, among others, failure of the product candidate to demonstrate safety or efficacy, the development of serious or life-threatening adverse events (or side effects) caused by or connected with exposure to the product candidate, difficulty in enrolling and maintaining subjects in the clinical trial, lack of sufficient supplies of the product candidate or comparator drug, and the failure of clinical investigators, trial monitors and other consultants, or trial subjects to comply with the trial plan or protocol. A clinical trial may fail because it did not include a sufficient number of patients to detect the endpoint being measured or reach statistical significance. A clinical trial may also fail because the dose(s) of the investigational drug included in the trial were either too low or too high to determine the optimal effect of the investigational drug in the disease setting.

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

***Serious complications or side effects have occurred, and may continue to occur, in connection with the use of our approved product and in clinical trials of some of our product candidates which could cause our regulatory approval to be revoked or otherwise negatively affected or lead to delay or discontinuation of development of our product candidates which could severely harm our business.***

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

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Our aflibercept (VEGF Trap) is being studied for the potential treatment of certain types of cancer and our VEGF Trap-Eye candidate is being studied in diseases of the eye. There are many potential safety concerns associated with significant blockade of vascular endothelial growth factor, or VEGF. These serious and potentially life-threatening risks, based on the clinical and preclinical experience of systemically delivered VEGF inhibitors, including the systemic delivery of the VEGF Trap, include bleeding, intestinal perforation, hypertension, and proteinuria. These serious side effects and other serious side effects have been reported in our systemic VEGF Trap studies in cancer and diseases of the eye. In addition, patients given infusions of any protein, including the VEGF Trap delivered through intravenous administration, may develop severe hypersensitivity reactions or infusion reactions. Other VEGF blockers have reported side effects that became evident only after large scale trials or after marketing approval and large number of patients were treated. These include side effects that we have not yet seen in our trials such as heart attack and stroke. These and other complications or side effects could harm the development of aflibercept for the treatment of cancer or VEGF Trap-Eye for the treatment of diseases of the eye.

We have tested ARCALYST™ in only a small number of patients with CAPS. As more patients begin to use our product and as we test it in new disease settings, new risks and side effects associated with ARCALYST™ may be discovered, and risks previously viewed as inconsequential could be determined to be significant. Like cytokine antagonists such as Kineret® (Amgen Inc.), Enbrel® (Immunex Corporation), and Remicade® (Centocor, Inc.), ARCALYST™ affects the immune defense system of the body by blocking some of its functions. Therefore, ARCALYST™ may interfere with the body's ability to fight infections. Treatment with Kineret® (Amgen), 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™. These or other complications or side effects could cause regulatory authorities to revoke approvals of ARCALYST™. 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™ in new disease settings. These side effects may also result in a reduction, or even the elimination, of sales of ARCALYST™ in approved indications.

***ARCALYST™ (rilonacept) and 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 that there can be no assurance that neutralizing antibodies will not be detected at a later date, in some cases even after pivotal clinical trials have been completed. Antibodies directed against the receptor domains of rilonacept were detected in patients with

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CAPS after treatment with ARCALYST™ (rilonacept). Nineteen of 55 subjects (35%) who received ARCALYST™ for at least 6 weeks tested positive for treatment-emerging binding antibodies on at least one occasion. To date, no side effects related to antibodies were observed in these subjects and there were no observed effects on drug efficacy or drug levels. It is possible that as we continue to test aflibercept and VEGF Trap-Eye with more sensitive assays in different patient populations and larger clinical trials, we will find that subjects given aflibercept and VEGF Trap-Eye develop antibodies to these product candidates, and may also experience side effects related to the antibodies, which could adversely impact the development of such candidates.

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

Changes in product formulations and manufacturing processes may be required as product candidates progress in clinical development and are ultimately commercialized. If we are unable to develop suitable product formulations or manufacturing processes to support large scale clinical testing of our product candidates, including aflibercept, VEGF Trap-Eye, and REGN88, we may be unable to supply necessary materials for our clinical trials, which would delay the development of our product candidates. Similarly, if we are unable to supply sufficient quantities of our product or develop product formulations suitable for commercial use, we will not be able to successfully commercialize our product candidates.

### **Risks Related to Intellectual Property**

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

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

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



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Our commercial success depends significantly on our ability to operate without infringing the patents and other proprietary rights of third parties. Other parties may allege that they have blocking patents to our products in clinical development, either because they claim to hold proprietary rights to the composition of a product or the way it is manufactured or used. Moreover, other parties may allege that they have blocking patents to antibody products made using our *VelocImmune* technology, either because of the way the antibodies are discovered or produced or because of a proprietary position covering an antibody or the antibody's target.

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

We are aware of patents and pending applications owned by Roche that claim antibodies to the interleukin-6 receptor and methods of treating rheumatoid arthritis with such antibodies. We are developing REGN88, an antibody to the interleukin-6 receptor, for the treatment of rheumatoid arthritis. Although we do not believe that REGN88 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 REGN88.

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. We cannot assure you that our products and/or actions in manufacturing and selling our product candidates will not infringe such patents.

In December 2003, we entered into a non-exclusive license agreement with Cellectis Inc. that granted us certain rights in a family of patents relating to homologous recombination. Cellectis now claims that our use of *VelocImmune* and our agreements with AstraZeneca, Astellas, and sanofi-aventis are outside the scope of our license from Cellectis. As a result, Cellectis claims that it has terminated our non-exclusive license agreement and has requested that we cease and desist from using the patents licensed from Cellectis. We disagree with Cellectis' position and are in discussions with Cellectis regarding this matter. If we are not able to resolve this dispute, Cellectis may commence a lawsuit against us, sanofi-aventis, our *VelocImmune* licensees, and our *VelociGene* customers alleging infringement of the patents we licensed from Cellectis.

Any patent holders could sue us for damages and seek to prevent us from manufacturing, selling, or developing our drug candidates, and a court may find that we are infringing validly issued patents of third parties. In the event that the manufacture, use, or sale of any of our clinical candidates infringes on the patents or violates other proprietary rights of third parties, we may be

prevented from pursuing product development, manufacturing, and commercialization of our drugs and may be required to pay costly damages. Such a result may materially harm our business, financial condition, and results of operations. Legal disputes are likely to be costly and time consuming to defend.

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

### **Regulatory and Litigation Risks**

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

We cannot sell or market products without regulatory approval. Although we obtained regulatory approval for ARCALYST™ (rilonacept) for the treatment of CAPS in the United States, we may be unable to obtain regulatory approval of ARCALYST™ in any other country or in any other indication. Regulatory agencies outside the United States may require additional information or data with respect to any future submission for ARCALYST™ for the treatment of CAPS.

If we do not obtain and maintain regulatory approval for our product candidates, including ARCALYST™ for the treatment of diseases other than CAPS, the value of our company and our results of operations will be harmed. In the United States, we must obtain and maintain approval from the United States Food and Drug Administration (FDA) for each drug we intend to sell. Obtaining FDA approval is typically a lengthy and expensive process, and approval is highly uncertain. Foreign governments also regulate drugs distributed in their country and approval in any country is likely to be a lengthy and expensive process, and approval is highly uncertain. Except for the recent FDA approval of ARCALYST™ for the treatment of CAPS, none of our product candidates has ever received regulatory approval to be marketed and sold in the United States or any other country. We may never receive regulatory approval for any of our product candidates.

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

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 includes all of the risks associated with FDA approval as well as country specific regulations. Whether or not we obtain FDA approval for a product in the United States, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials or marketing of ARCALYST™ for the treatment of CAPS or any of our product candidates in those countries.

***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. We may be subject to claims by CAPS patients who use ARCALYST™ that they have been injured by a side effect associated with the drug. Any informed consent or waivers obtained from people who sign up for our clinical trials may not protect us from liability or the cost of litigation. Our product liability insurance may not cover all potential liabilities or may not completely cover any liability arising from any such litigation. Moreover, we may not have access to liability insurance or be able to maintain our insurance on acceptable terms.

***If we market and sell ARCALYST™ (rilonacept) in a way that violates federal or state fraud and abuse 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, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any health care item or service reimbursable under Medicare, Medicaid, or other federally or state financed health care programs.

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, or 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.

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Even if we are not determined to have violated these laws, government investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which would also harm our financial 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 subject to challenge under one or more of such laws.

In recent years, several states and localities, including California, the District of Columbia, Maine, 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 legislation is being considered in other states. 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 action and fines and other penalties, and could receive adverse publicity.

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

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

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

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

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

As directed by Section 404 of the Sarbanes-Oxley Act of 2002, the SEC adopted rules requiring public companies to include a report of management on the Company's internal control over financial reporting in their annual reports on Form 10-K that contains an assessment by management of the effectiveness of our internal control over financial reporting. In addition, the independent registered public accounting firm auditing our financial statements must attest to and report on the effectiveness of our internal control over financial reporting. Our independent registered public accounting firm provided us with an unqualified report as to the effectiveness of our internal control over financial reporting as of December 31, 2007, which report is included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2007 which was filed with the Securities and Exchange Commission on February 27, 2008. However, we cannot assure you that management or our independent registered public accounting firm will be able to provide such an unqualified report as of future year-ends. In this event, investors could lose confidence in the reliability of our financial statements, which could result in a decrease in the market value of our common stock. In addition, if it is determined that deficiencies in the design or operation of internal controls exist and that they are reasonably likely to adversely affect our ability to record, process, summarize, and report financial information, we would likely incur additional costs to remediate these deficiencies and the costs of such remediation could be material.

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

***If our antibody collaboration with sanofi-aventis is terminated, our business operations 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 the funding from sanofi-aventis to support our target discovery and antibody research and development programs. Sanofi-aventis has committed to pay up to \$475.0 million between 2008 and 2012 to fund our efforts to identify and validate drug discovery targets and pre-clinically develop fully human monoclonal antibodies against such targets. In addition, sanofi-aventis funds almost all of the development expenses incurred by both companies in connection with the clinical development of antibodies that sanofi-aventis elects to co-develop with us. We rely on sanofi-aventis to fund these activities. In addition, with respect to those antibodies that sanofi-aventis elects to co-develop with us, such as REGN88, we rely on sanofi-aventis to lead much of the clinical development efforts and assist with obtaining regulatory approval, particularly outside the United States. We also rely on sanofi-aventis to lead the commercialization efforts to support all of the antibody products that are co-developed by sanofi-aventis and us. If sanofi-aventis 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 our antibody products. Sanofi-aventis may terminate the collaboration for our material breach or, in the case of the discovery agreement, if certain minimal criteria for the discovery program are not achieved by December 31, 2010. If sanofi-aventis terminates the antibody collaboration or fails to comply with its payment obligations thereunder, our business, financial condition, and results of operations would be materially harmed. We would be required to either expend substantially

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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. While we cannot assure you that any of the antibodies from this collaboration will ever be successfully developed and commercialized, if sanofi-aventis 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-aventis for aflibercept (VEGF Trap) is terminated, or sanofi-aventis materially breaches its obligations thereunder, our business, operations and financial condition, and our ability to develop, manufacture, and commercialize aflibercept in the time expected, or at all, would be materially harmed.***

We rely heavily on sanofi-aventis to lead much of the development of aflibercept. Sanofi-aventis funds all of the development expenses incurred by both companies in connection with the aflibercept program. If the aflibercept program continues, we will rely on sanofi-aventis to assist with funding the aflibercept program, provide commercial manufacturing capacity, enroll and monitor clinical trials, obtain regulatory approval, particularly outside the United States, and lead the commercialization of aflibercept. While we cannot assure you that aflibercept will ever be successfully developed and commercialized, if sanofi-aventis does not perform its obligations in a timely manner, or at all, our ability to develop, manufacture, and commercialize aflibercept in cancer indications will be significantly adversely affected. Sanofi-aventis has the right to terminate its collaboration agreement with us at any time upon twelve months advance notice. If sanofi-aventis were to terminate its collaboration agreement with us, we would not have the resources or skills to replace those of our partner, which could 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 aflibercept 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-aventis collaboration agreement for aflibercept would create substantial new and additional risks to the successful development and commercialization of aflibercept.

***If our collaboration with Bayer HealthCare for VEGF Trap-Eye is terminated, or Bayer HealthCare materially breaches its obligations thereunder, our business, operations and financial condition, and our ability to develop and commercialize VEGF Trap-Eye in the time expected, or at all, would be materially harmed.***

We rely heavily on Bayer HealthCare to assist with the development of VEGF Trap-Eye. Under our agreement with them, Bayer HealthCare is required to fund approximately half of the development expenses incurred by both companies in connection with the global VEGF Trap-Eye development program. If the VEGF Trap-Eye program continues, we will rely on Bayer HealthCare to assist with funding the VEGF Trap-Eye development program, lead the development of VEGF Trap-Eye 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 VEGF Trap-Eye outside the United States using its sales force. While we cannot assure you that VEGF Trap-Eye will ever be successfully developed and commercialized, if Bayer HealthCare does not perform

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its obligations in a timely manner, or at all, our ability to develop, manufacture, and commercialize VEGF Trap-Eye outside the United States will be significantly adversely affected. Bayer HealthCare has the right to terminate its collaboration agreement with us at any time upon six or twelve months advance notice, depending on the circumstances giving rise to termination. If Bayer HealthCare were to terminate its collaboration agreement with us, we would not have the resources or skills to replace those of our partner, which could 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 commercialization of VEGF Trap-Eye outside the United States and result in substantial additional costs to us. We 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 VEGF Trap-Eye.

### ***Our collaborators and service providers may fail to perform adequately in their efforts to support the development, manufacture, and commercialization of ARCALYST™ (rilonacept) and our drug candidates.***

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

We rely on third party service providers to support the distribution of ARCALYST™ and many other related activities in connection with the commercialization of ARCALYST™ for the treatment of CAPS. We cannot be certain that these third parties will perform adequately. If these service providers do not perform their services adequately, our efforts to market and sell ARCALYST™ for the treatment of CAPS will not be successful.

### **Risks Related to the Manufacture of Our Product Candidates**

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

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

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

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

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

We have large-scale manufacturing operations in Rensselaer, New York. We use our facilities to produce bulk product for clinical and preclinical candidates for ourselves and our collaborations. If our clinical candidates are discontinued, we will have to absorb one hundred percent of related overhead costs and inefficiencies.

***We sole source all of our bulk drug materials from our manufacturing facility in Rensselaer, New York; certain of our raw materials and manufacturing services are single-sourced from third parties; third-party supply failures or a business interruption at our manufacturing facility in Rensselaer, New York could adversely affect our ability to supply our products.***

We manufacture all of our bulk drug materials for ARCALYST™ and our product candidates at our manufacturing facility in Rensselaer, New York. We would be unable to supply our product requirements if we were to cease production due to regulatory requirements or action, business interruptions, labor shortages or disputes, contaminations, or other problems at the facility.

Certain raw materials necessary for manufacturing and formulation of ARCALYST™ and our product candidates are provided by single-source unaffiliated third-party suppliers. In addition, we rely on certain third parties to perform filling, finishing, distribution, and other services related to the manufacture of our products. 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, business interruptions, or labor shortages or disputes. This, in turn, could materially and adversely affect our ability to manufacture or supply



ARCALYST™ or our product candidates for use in clinical trials, which could materially and adversely affect our business and future prospects.

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

#### **Risks Related to Commercialization of Products**

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

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

***There may be too few patients with CAPS to profitably commercialize ARCALYST™ (rilonacept) in this indication.***

Our only approved product is ARCALYST™ for the treatment of CAPS, a group of rare, inherited auto-inflammatory diseases. These rare diseases affect a very small group of people. The incidence of CAPS has been reported to be approximately 1 in 1,000,000 people in the United States. As a result, there may be too few patients with CAPS to profitably commercialize ARCALYST™ in this indication.

***Even if our product candidates are approved for marketing, their commercial success is highly uncertain because our competitors have received approval for products with the same mechanism of action, and competitors may get to the marketplace with better or lower cost drugs.***

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There is substantial competition in the biotechnology and pharmaceutical industries from pharmaceutical, biotechnology, and chemical companies. Many of our competitors have substantially greater research, preclinical and clinical product development and manufacturing capabilities, and financial, marketing, and human resources than we do. Our smaller competitors may also enhance their competitive position if they acquire or discover patentable inventions, form collaborative arrangements, or merge with large pharmaceutical companies. Even if we achieve product commercialization, our competitors have achieved, and may continue to achieve, product commercialization before our products are approved for marketing and sale.

Genentech has an approved VEGF antagonist, Avastin® (Genentech), on the market for treating certain cancers and many different pharmaceutical and biotechnology companies are working to develop competing VEGF antagonists, including Novartis, OSI Pharmaceuticals, Inc., and Pfizer Inc. Many of these molecules are farther along in development than aflibercept and may offer competitive advantages over our molecule. Novartis has an ongoing Phase 3 clinical development program evaluating an orally delivered VEGF tyrosine kinase inhibitor in different cancer settings. Each of Pfizer and Onyx Pharmaceuticals, Inc., (together with its partner Bayer HealthCare) has received approval from the FDA to market and sell an oral medication that targets tumor cell growth and new vasculature formation that fuels the growth of tumors. The marketing approvals for Genentech's VEGF antagonist, Avastin® (Genentech), and their extensive, ongoing clinical development plan for Avastin® (Genentech) in other cancer indications, make it more difficult for us to enroll patients in clinical trials to support aflibercept and to obtain regulatory approval of aflibercept in these cancer settings. This may delay or impair our ability to successfully develop and commercialize aflibercept. In addition, even if aflibercept is ever approved for sale for the treatment of certain cancers, it will be difficult for our drug to compete against Avastin® (Genentech) and the FDA approved kinase inhibitors, because doctors and patients will have significant experience using these medicines. In addition, an oral medication may be considerably less expensive for patients than a biologic medication, providing a competitive advantage to companies that market such products.

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

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The availability of highly effective FDA approved TNF-antagonists such as Enbrel® (Immunex), Remicade® (Centocor), and Humira® (Abbott Laboratories), and the IL-1 receptor antagonist Kineret® (Amgen), and other marketed therapies makes it more difficult to successfully develop and commercialize ARCALYST™. This is one of the reasons we discontinued the development of ARCALYST™ in adult rheumatoid arthritis. In addition, even if ARCALYST™ 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 will have significant experience using these effective medicines. Moreover, in such indications these approved therapeutics may offer competitive advantages over ARCALYST™, 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 interleukin-1 or inhibit the signaling of interleukin-1. For example, Eli Lilly and Company, Xoma Ltd., and Novartis are each developing antibodies to interleukin-1 and Amgen is developing an antibody to the interleukin-1 receptor. Novartis has commenced advanced clinical testing of its IL-1 antibody in Muckle-Wells Syndrome, which is part of the group of rare genetic diseases called CAPS. Novartis recently announced that its IL-1 antibody demonstrated long-lasting clinical remission in patients with CAPS and that its clinical candidate could develop into a major therapeutic advance in the treatment of CAPS. Novartis' IL-1 antibody and these other drug candidates could offer competitive advantages over ARCALYST™. The successful development of these competing molecules could delay or impair our ability to successfully develop and commercialize ARCALYST™.

We are developing REGN88 for the treatment of rheumatoid arthritis. The availability of highly effective FDA approved TNF-antagonists such as Enbrel® (Immunex), Remicade® (Centocor), and Humira® (Abbott), and other marketed therapies makes it more difficult to successfully develop and commercialize REGN88. REGN88 is a human monoclonal antibody targeting the interleukin-6 receptor. Roche is developing an antibody against the interleukin-6 (IL-6) receptor. Roche's antibody has completed Phase 3 clinical trials and is the subject of a filed Biologics License Application with the FDA. Roche's IL-6 receptor antibody, other clinical candidates in development, and drugs now or in the future on the market to treat rheumatoid arthritis could offer competitive advantages over REGN88. This could delay or impair our ability to successfully develop and commercialize REGN88.

***The successful commercialization of ARCALYST™ (rilonacept) and our product candidates will depend on obtaining coverage and reimbursement for use of these products from third-party payers and these payers may not agree to cover or reimburse for use of our products.***

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

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of treatment before covering a particular drug. Payers may especially impose these obstacles to coverage on higher-priced drugs, as our product candidates are likely to be.

We market and sell ARCALYST™ (rilonacept) in the United States for the treatment of a group of rare genetic disorders called CAPS. There may be too few patients with CAPS to profitably commercialize ARCALYST™. Physicians may not prescribe ARCALYST™, and CAPS patients may not be able to afford ARCALYST™, if third party payers do not agree to reimburse the cost of ARCALYST™ therapy and this would adversely affect our ability to commercialize ARCALYST™ profitably.

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

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

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

### **Risk Related to Employees**

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

We are highly dependent on certain of our executive officers. If we are not able to retain any of these persons or our Chairman, our business may suffer. In particular, we depend on the services of P. Roy Vagelos, M.D., the Chairman of our board of directors, Leonard Schleifer, M.D., Ph.D., our President and Chief Executive Officer, George D. Yancopoulos, M.D., Ph.D.,

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our Executive Vice President, Chief Scientific Officer and President, Regeneron Research Laboratories, and Neil Stahl, Ph.D., our Senior Vice President, Research and Development Sciences. There is intense competition in the biotechnology industry for qualified scientists and managerial personnel in the development, manufacture, and commercialization of drugs. We may not be able to continue to attract and retain the qualified personnel necessary for developing our business.

### **Risks Related to Our Common Stock**

#### ***Our stock price is extremely volatile.***

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

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

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

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

A small number of our shareholders beneficially own a substantial amount of our common stock. As of April 15, 2008, our eight largest shareholders beneficially owned 57.7% of our outstanding shares of Common Stock, assuming, in the case of Leonard S. Schleifer, M.D. Ph.D., our Chief Executive Officer, and P. Roy Vagelos, M.D., our Chairman, the conversion of their Class A Stock into Common Stock and the exercise of all options held by them which are exercisable within 60 days of April 15, 2008. As of April 15, 2008, sanofi-aventis beneficially owned 14,799,552 shares of Common Stock, representing approximately 19.3% of the shares of Common Stock then outstanding. Under our investor agreement with sanofi-aventis, sanofi-aventis may not sell these shares until December 20, 2012 except under limited circumstances and subject to earlier termination rights of these restrictions upon the occurrence of certain

events. Notwithstanding these restrictions, if sanofi-aventis, or our other significant shareholders or we, sell substantial amounts of our Common Stock in the public market, or the perception that such sales may occur exists, the market price of our Common Stock could fall. Sales of Common Stock by our significant shareholders, including sanofi-aventis, also might make it more difficult for us to raise funds by selling equity or equity-related securities in the future at a time and price that we deem appropriate.

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

Holders of Class A Stock, who are generally the shareholders who purchased their stock from us before our initial public offering, are entitled to ten votes per share, while holders of Common Stock are entitled to one vote per share. As of April 15, 2008, holders of Class A Stock held 22.7% of the combined voting power of all of Common Stock and Class A Stock then outstanding. These shareholders, if acting together, would be in a position to significantly influence the election of our directors and to effect or prevent certain corporate transactions that require majority or supermajority approval of the combined classes, including mergers and other business combinations. This may result in our company taking corporate actions that you may not consider to be in your best interest and may affect the price of our Common Stock. As of April 15, 2008:

- our current executive officers and directors beneficially owned 12.5% 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 April 15, 2008, and 27.6% 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 April 15, 2008; and
- our eight largest shareholders beneficially owned 57.7% of our outstanding shares of Common Stock, assuming, in the case of Leonard S. Schleifer, M.D., Ph.D., our Chief Executive Officer, and P. Roy Vagelos, M.D., our Chairman, the conversion of their Class A Stock into Common Stock and the exercise of all options held by them which are exercisable within 60 days of April 15, 2008. In addition, these eight shareholders held 61.0% of the combined voting power of our outstanding shares of Common Stock and Class A Stock, assuming the exercise of all options held by our Chief Executive Officer and our Chairman which are exercisable within 60 days of April 15, 2008.

Pursuant to an investor agreement, sanofi-aventis has agreed to vote its shares, at sanofi-aventis' 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.

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***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-aventis, could deter, delay, or prevent an acquisition or other “change in control” of us and could adversely affect the price of our Common Stock.***

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

- authorization to issue “blank check” preferred stock, which is preferred stock that can be created and issued by the board of directors without prior shareholder approval, with rights senior to those of our common shareholders;
- a staggered board of directors, so that it would take three successive annual meetings to replace all of our directors;
- a requirement that removal of directors may only be effected for cause and only upon the affirmative vote of at least eighty percent (80%) of the outstanding shares entitled to vote for directors, as well as a requirement that any vacancy on the board of directors may be filled only by the remaining directors;
- any action required or permitted to be taken at any meeting of shareholders may be taken without a meeting, only if, prior to such action, all of our shareholders consent, the effect of which is to require that shareholder action may only be taken at a duly convened meeting;
- any shareholder seeking to bring business before an annual meeting of shareholders must provide timely notice of this intention in writing and meet various other requirements; and
- under the New York Business Corporation Law, in addition to certain restrictions which may apply to “business combinations” involving the Company and an “interested shareholder”, a plan of merger or consolidation of the Company must be approved by two-thirds of the votes of all outstanding shares entitled to vote thereon. See the risk factor immediately above captioned “*Our existing shareholders may be able to exert significant influence over matters requiring shareholder approval.*”

Until the later of the fifth anniversaries of the expiration or earlier termination of our antibody collaboration agreements with sanofi-aventis or our aflibercept collaboration with sanofi-aventis, sanofi-aventis will be bound by certain “standstill” provisions, which contractually prohibit sanofi-aventis from acquiring more than certain specified percentages of the Company’s Class A Stock and Common Stock (taken together) or otherwise seeking to obtain control of the 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 the Company. Many of our stock options issued under our 2000 Long-Term Incentive Plan may become fully vested in connection with a “change in control” of our company, as defined in the plan.

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### Item 6. Exhibits

(a) Exhibits

<u>Exhibit Number</u>	<u>Description</u>
12.1	- Statement re: computation of ratio of earnings to combined fixed charges.
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.



**SIGNATURE**

Pursuant to the requirements 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.

Date: May 2, 2008

By: /s/ Murray A. Goldberg

Murray A. Goldberg  
Senior Vice President, Finance & Administration,  
Chief Financial Officer, Treasurer, and  
Assistant Secretary  
(Principal Financial Officer and  
Duly Authorized Officer)

**Regeneron Pharmaceuticals, Inc.**  
**Computation of Ratio of Earnings to Combined Fixed Charges**  
*(Dollars in thousands)*

	Years ended December 31,					Three months ended March 31, 2008
	2003	2004	2005	2006	2007	
<b>Earnings:</b>						
Income (loss) from continuing operations before income (loss) from equity investee	\$(107,395)	\$41,565	\$(95,456)	\$(103,150)	\$(105,600)	\$(11,618)
Fixed charges	14,108	14,060	13,687	13,643	13,708	3,434
Amortization of capitalized interest	33	78	78	73	23	5
Interest capitalized	(276)	—	—	—	—	—
<b>Adjusted earnings</b>	<b>\$ (93,530)</b>	<b>\$55,703</b>	<b>\$(81,691)</b>	<b>\$ (89,434)</b>	<b>\$ (91,869)</b>	<b>\$ (8,179)</b>
<b>Fixed charges:</b>						
Interest expense	\$ 11,932	\$12,175	\$ 12,046	\$ 12,043	\$ 12,043	\$ 3,011
Interest capitalized	276	—	—	—	—	—
Assumed interest component of rental charges	1,900	1,885	1,641	1,600	1,665	423
<b>Total fixed charges</b>	<b>\$ 14,108</b>	<b>\$14,060</b>	<b>\$ 13,687</b>	<b>\$ 13,643</b>	<b>\$ 13,708</b>	<b>\$ 3,434</b>
<b>Ratio of earnings to fixed charges</b>	<b>(A)</b>	<b>3.96</b>	<b>(A)</b>	<b>(A)</b>	<b>(A)</b>	<b>(A)</b>

(A) Due to the registrant's losses for the years ended December 31, 2003, 2005, 2006, and 2007, and for the three months ended March 31, 2008, the ratio coverage was less than 1:1. To achieve a coverage ratio of 1:1, the registrant must generate additional earnings of the amounts shown in the table below.

	Years ended December 31,				Three months ended March 31, 2008
	2003	2005	2006	2007	
Coverage deficiency	\$107,638	\$95,378	\$103,077	\$105,577	\$11,613

**Certification of CEO Pursuant to  
Rule 13a-14(a) under the Securities Exchange Act  
of 1934, as Adopted Pursuant to  
Section 302 of the Sarbanes-Oxley Act of 2002**

I, Leonard S. Schleifer, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Regeneron Pharmaceuticals, Inc.;
  2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
  3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations, and cash flows of the registrant as of, and for, the periods presented in this report;
  4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
-

- d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 2, 2008

/s/ Leonard S. Schleifer

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Leonard S. Schleifer, M.D., Ph.D.

President and Chief Executive Officer

**Certification of CFO Pursuant to  
Rule 13a-14(a) under the Securities Exchange Act  
of 1934, as Adopted Pursuant to  
Section 302 of the Sarbanes-Oxley Act of 2002**

I, Murray A. Goldberg, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Regeneron Pharmaceuticals, Inc.;
  2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
  3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations, and cash flows of the registrant as of, and for, the periods presented in this report;
  4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
    - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
    - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
    - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
-

- d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
- a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
  - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: May 2, 2008

/s/ Murray A. Goldberg

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

**Certification of CEO and CFO Pursuant to  
18 U.S.C. Section 1350,  
As Adopted Pursuant to  
Section 906 of the Sarbanes-Oxley Act of 2002**

In connection with the Quarterly Report of Regeneron Pharmaceuticals, Inc. (the "Company") on Form 10-Q for the quarterly period ended March 31, 2008 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), Leonard S. Schleifer, M.D., Ph.D., as Chief Executive Officer of the Company, and Murray A. Goldberg, as Chief Financial Officer of the Company, each hereby certifies, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, to the best of his knowledge, that:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

/s/ Leonard S. Schleifer  
Leonard S. Schleifer, M.D., Ph.D.  
Chief Executive Officer  
May 2, 2008

/s/ Murray A. Goldberg  
Murray A. Goldberg  
Chief Financial Officer  
May 2, 2008