

REGENERON PHARMACEUTICALS INC

Form 10-Q

November 05, 2008

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**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 September 30, 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

13-3444607

(State or other jurisdiction of  
incorporation or organization)

(I.R.S. Employer Identification No.)

777 Old Saw Mill River Road  
Tarrytown, New York

10591-6707

(Address of principal executive offices)

(Zip Code)

(914) 347-7000

(Registrant's telephone number, including area code)

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 the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer <input checked="" type="checkbox"/>	Accelerated filer <input type="checkbox"/>	Non-accelerated filer <input type="checkbox"/> (Do not check if a smaller reporting company)	Smaller reporting company <input type="checkbox"/>
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Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act).

Yes ☐ No ☒

Number of shares outstanding of each of the registrant's classes of common stock as of October 15, 2008:

Class of Common Stock

Number of Shares

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Class A Stock, \$0.001 par value	2,254,698
Common Stock, \$0.001 par value	77,392,971

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**September 30, 2008**

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	<b>September 30, 2008</b>	<b>December 31, 2007</b>
<b>ASSETS</b>		
Current assets		
Cash and cash equivalents	\$ 314,684	\$ 498,925
Marketable securities	348,924	267,532
Accounts receivable from the sanofi-aventis Group	37,744	14,244
Accounts receivable other	4,462	4,076
Prepaid expenses and other current assets	9,726	13,052
Total current assets	715,540	797,829
Restricted cash	1,650	1,600
Marketable securities	27,603	78,222
Property, plant, and equipment, at cost, net of accumulated depreciation and amortization	72,825	58,304
Other assets	8,273	303
Total assets	\$ 825,891	\$ 936,258
<b>LIABILITIES and STOCKHOLDERS EQUITY</b>		
Current liabilities		
Accounts payable and accrued expenses	\$ 41,887	\$ 39,232
Deferred revenue from sanofi-aventis, current portion	19,017	18,855
Deferred revenue other, current portion	39,364	25,577
Notes payable	117,503	200,000
Total current liabilities	217,771	283,664
Deferred revenue from sanofi-aventis	112,290	126,431
Deferred revenue other	56,012	65,896
Other long term liabilities	2,885	0
Total liabilities	388,958	475,991
Commitments and contingencies		
Stockholders equity		
Preferred stock, \$.01 par value; 30,000,000 shares authorized; issued and outstanding-none		

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Class A Stock, convertible, \$.001 par value; 40,000,000 shares authorized; shares issued and outstanding 2,254,698 in 2008 and 2,260,266 in 2007	2	2
Common Stock, \$.001 par value; 160,000,000 shares authorized; shares issued and outstanding 77,367,679 in 2008 and 76,592,218 in 2007	77	77
Additional paid-in capital	1,285,223	1,253,235
Accumulated deficit	(844,409)	(793,217)
Accumulated other comprehensive income (loss)	(3,960)	170
Total stockholders' equity	436,933	460,267
Total liabilities and stockholders' equity	\$ 825,891	\$ 936,258

**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 September 30,</b>		<b>Nine months ended September 30,</b>	
	<b>2008</b>	<b>2007</b>	<b>2008</b>	<b>2007</b>
Revenues				
Contract research and development from sanofi-aventis	\$ 42,006	\$ 9,182	\$ 116,346	\$ 34,486
Other contract research and development	10,872	3,129	33,568	7,387
Technology licensing	10,000	10,000	30,000	18,421
Net product sales	2,706		2,706	
	65,584	22,311	182,620	60,294
Expenses				
Research and development	73,855	51,689	201,702	136,788
Selling, general, and administrative	11,368	9,289	35,857	26,426
Cost of goods sold	292		292	
	85,515	60,978	237,851	163,214
Loss from operations	(19,931)	(38,667)	(55,231)	(102,920)
Other income (expense)				
Investment income	3,674	5,840	15,513	19,424
Interest expense	(1,772)	(3,011)	(7,457)	(9,033)
Loss on early extinguishment of debt	(7)		(938)	
	1,895	2,829	7,118	10,391
Net loss before income tax expense	(18,036)	(35,838)	(48,113)	(92,529)
Income tax expense	3,079		3,079	
Net loss	\$ (21,115)	\$ (35,838)	\$ (51,192)	\$ (92,529)
Net loss per share amounts, basic and diluted	\$ (0.27)	\$ (0.54)	\$ (0.65)	\$ (1.40)
Weighted average shares outstanding, basic and diluted	78,937	66,069	78,706	65,861

**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 nine months ended September 30, 2008**  
*(In thousands)*

	Class A Stock		Common Stock		Additional Paid-in	Accumulated Deficit	Accumulated Other Comprehensive Income (Loss)	Stockholders' Equity	Total
	Shares	Amount	Shares	Amount	Capital	Deficit	(Loss)		Loss
<b>Balance, December 31, 2007</b>	2,260	\$ 2	76,592	\$ 77	\$ 1,253,235	\$ (793,217)	\$ 170	\$ 460,267	
Issuance of Common Stock in connection with exercise of stock options, net of shares tendered			711		6,165			6,165	
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	(5)		5						
Stock-based compensation expense					24,716			24,716	
Net loss						(51,192)		(51,192)	\$ (51,192)
Change in net unrealized gain (loss) on marketable securities							(4,130)	(4,130)	(4,130)
<b>Balance, September 30, 2008</b>	2,255	\$ 2	77,367	\$ 77	\$ 1,285,223	\$ (844,409)	\$ (3,960)	\$ 436,933	\$ (55,322)

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>Nine months ended September 30,</b>	
	<b>2008</b>	<b>2007</b>
Cash flows from operating activities		
Net loss	\$ (51,192)	\$ (92,529)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization	8,661	8,588
Non-cash compensation expense	24,716	20,538
Loss on early extinguishment of debt	938	
Net realized loss on marketable securities	1,166	803
Changes in assets and liabilities		
Increase in accounts receivable	(23,886)	(3,475)
Increase in prepaid expenses and other assets	(5,279)	(11,876)
(Decrease) increase in deferred revenue	(10,076)	46,832
Increase in accounts payable, accrued expenses, and other liabilities	1,706	7,674
Total adjustments	(2,054)	69,084
Net cash used in operating activities	(53,246)	(23,445)
Cash flows from investing activities		
Purchases of marketable securities	(478,276)	(478,209)
Sales or maturities of marketable securities	443,587	363,739
Capital expenditures	(19,117)	(7,716)
Increase in restricted cash	(50)	
Net cash used in investing activities	(53,856)	(122,186)
Cash flows from financing activities		
Repayment of long-term debt	(83,304)	
Net proceeds from the issuance of Common Stock	6,165	5,171
Net cash (used in) provided by financing activities	(77,139)	5,171
Net decrease in cash and cash equivalents	(184,241)	(140,460)
Cash and cash equivalents at beginning of period	498,925	237,876
Cash and cash equivalents at end of period	\$ 314,684	\$ 97,416

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

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**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.

Included in research and development expenses is the Company's share of VEGF Trap-Eye development expenses incurred by Bayer HealthCare LLC, including the Company's share of Bayer HealthCare's estimated VEGF Trap-Eye development expenses for the most recent interim fiscal quarter. Bayer HealthCare's estimate is reconciled to its actual expenses for such quarter in the subsequent interim fiscal quarter and the Company's share of VEGF Trap-Eye development expenses incurred by Bayer HealthCare is adjusted accordingly. During the three and nine months ended September 30, 2008, the Company recognized cost sharing of Bayer HealthCare VEGF Trap-Eye development expenses of \$3.6 million and \$19.0 million, respectively. For the three months ended September 30, 2008, cost sharing of Bayer HealthCare development expenses consists of \$4.1 million of estimated third quarter expense less a \$0.5 million adjustment to reconcile Bayer HealthCare's actual second quarter 2008 VEGF Trap-Eye development expenses to its prior estimate.

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

***Product Revenue***

In March 2008, ARCALYST® (rilonacept) became available for prescription in the United States for the treatment of Cryopyrin-Associated Periodic Syndromes (CAPS). During the three and nine months ended September 30, 2008, the Company shipped \$4.3 million and \$6.7 million, respectively, of ARCALYST to its distributors. The Company recognizes 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 the Company has no further performance obligations. Revenues from product sales are recorded net of applicable provisions for prompt pay discounts, product returns, estimated rebates payable under governmental programs (including Medicaid), distribution fees, and other sales-related costs.

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The Company accounts 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. We review our estimates of rebates payable each period and record any necessary adjustments in the current period's net product sales.

During the three and nine months ended September 30, 2008, the Company recognized as revenue \$2.7 million of ARCALYST® (rilonacept) net product sales for which both the right of return no longer exists and rebates can be reasonably estimated. At September 30, 2008, deferred revenue related to ARCALYST net product sales totaled \$3.8 million.

***Inventory***

The Company began capitalizing inventory costs associated with commercial supplies of ARCALYST subsequent to receipt of marketing approval from the U.S. Food and Drug Administration ( FDA ) in February 2008. Costs for manufacturing supplies of ARCALYST prior to receipt of FDA approval were recognized as research and development expenses in the period that the costs were incurred. Therefore, these costs are not being included in cost of goods sold when revenue is recognized from the sale of those supplies of ARCALYST. For the three and nine months ended September 30, 2008, ARCALYST cost of goods sold totaled \$0.3 million. At September 30, 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 and nine months ended September 30, 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 September 30,	
	2008	2007
Net loss (Numerator)	\$ (21,115)	\$ (35,838)
Weighted-average shares, in thousands (Denominator)	78,937	66,069
Basic and diluted net loss per share	\$ (0.27)	\$ (0.54)

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	Nine Months Ended September 30,	
	2008	2007
Net loss (Numerator)	\$ (51,192)	\$ (92,529)
Weighted-average shares, in thousands (Denominator)	78,706	65,861
Basic and diluted net loss per share	\$ (0.65)	\$ (1.40)

Shares issuable upon the exercise of stock options, vesting of restricted stock awards, and conversion of convertible debt, which have been excluded from the September 30, 2008 and 2007 diluted per share amounts because their effect would have been antidilutive, include the following:

	Three months ended September 30,	
	2008	2007
Stock Options:		
Weighted average number, in thousands	17,454	15,153
Weighted average exercise price	\$ 17.31	\$ 16.01
Restricted Stock:		
Weighted average number, in thousands	500	
Convertible Debt:		
Weighted average number, in thousands	3,890	6,611
Conversion price	\$ 30.25	\$ 30.25

	Nine months ended September 30,	
	2008	2007
Stock Options:		
Weighted average number, in thousands	17,572	15,308
Weighted average exercise price	\$ 17.24	\$ 15.86
Restricted Stock:		
Weighted average number, in thousands	500	
Convertible Debt:		
Weighted average number, in thousands	5,450	6,611
Conversion price	\$ 30.25	\$ 30.25

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**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:

Included in accounts payable and accrued expenses at September 30, 2008 and December 31, 2007 were \$5.1 million and \$1.7 million, respectively, of accrued capital expenditures. Also included in accounts payable and accrued expenses at September 30, 2008 was \$1.5 million in connection with a forward contract to purchase a marketable security. Included in accounts payable and accrued expenses at September 30, 2007 and December 31, 2006 were \$0.9 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 both September 30, 2008 and December 31, 2007 was \$2.2 million of accrued interest income. Included in marketable securities at September 30, 2007 and December 31, 2006 were \$2.5 million and \$1.5 million, respectively, of accrued interest income.

**5. Fair Value of Financial Assets**

The Company considers its marketable securities, which consist primarily of U.S. government, corporate, and asset-backed securities, to be available-for-sale, as defined by SFAS 115, *Accounting for Certain Investments in Debt and Equity Securities*. These assets are carried at fair value and the unrealized gains and losses are included in other accumulated comprehensive income (loss) as a separate component of stockholders' equity. If the decline in the value of a marketable security in the Company's investment portfolio is deemed to be other-than-temporary, the Company writes down the security to its current fair value and recognizes a loss that is charged against income.

On a quarterly basis, the Company reviews its portfolio of marketable securities, using both quantitative and qualitative factors, to determine if declines in fair value below cost are other-than-temporary. Such factors include the length of time and the extent to which market value has been less than cost, financial condition and near-term prospects of the issuer, recommendations of investment advisors, and forecasts of economic, market, or industry trends. This review process also includes an evaluation of the Company's ability and intent to hold individual securities until they mature or their full cost can be recovered. This review is subjective and requires a high degree of judgment.

As a result of the Company's quarterly reviews of its marketable securities portfolio, during the three and nine months ended September 30, 2008, the Company recorded charges for other-

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than-temporary impairment of its marketable securities totaling \$1.7 million and \$2.3 million, respectively, as described below. However, the current economic environment, the deterioration in the credit quality of some of the issuers of securities that the Company holds, and the recent volatility of securities markets increase the risk that there may be further declines in the market value of marketable securities in the Company's investment portfolio and that such declines may result in additional charges against income in future periods for other-than-temporary impairments, and such amounts may be material.

In September 2006, the Financial Accounting Standards Board (FASB) 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. In addition, in October 2008, the FASB issued FASB Staff Position (FSP) 157-3, *Determining the Fair Value of a Financial Asset When the Market for That Asset Is Not Active*, which clarifies the application of SFAS 157 in a market that is not active. FSP 157-3 also reaffirms the notion of fair value as an exit price as of the measurement date. FSP 157-3 was effective upon issuance for financial statements that have not yet been issued and adopted by the Company for the quarter ended September 30, 2008.

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.

The Company's assets that are measured at fair value on a recurring basis, and subject to the disclosure requirements of SFAS 157 at September 30, 2008, were as follows:

Description	Fair Value at September 30, 2008	Fair Value Measurements at Reporting Date Using Significant		
		Quoted Prices in Active Markets for Identical Assets (Level 1)	Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Available-for-sale marketable securities	\$376,527		\$ 376,257	\$ 270

The Company held no Level 1 marketable securities during the three or nine months ended September 30, 2008.



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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. During the third quarter of 2008, deterioration in the credit quality of a marketable security from one issuer subjected the Company to the risk of not being able to recover the security's \$2.0 million carrying value. As a result, the Company recognized a \$1.7 million charge related to this Level 2 marketable security, which the Company considered to be other than temporarily impaired.

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. During the nine months ended September 30, 2008, the Company recognized a \$0.5 million charge related to a Level 3 marketable security which the Company considered to be other than temporarily impaired.

Changes in marketable securities included in Level 3 above during the three months ended September 30, 2008 were as follows:

	Level 3 marketable securities
Balance July 1, 2008	\$ 4,995
Settlements	(5,665)
Realized gain	940
Balance September 30, 2008	\$ 270

Changes in marketable securities included in Level 3 above during the nine months ended September 30, 2008 were as follows:

	Level 3 marketable securities
Balance January 1, 2008	\$ 7,950
Settlements	(8,090)
Realized gain	940
Impairments	(530)
Balance September 30, 2008	\$ 270

There were no unrealized gains or losses related to the Company's Level 3 marketable securities for the three and nine months ended September 30, 2008. In addition, there were no purchases of Level 3 marketable securities and no transfers of marketable securities between the Level 2 and Level 3 classifications during the three and nine months ended September 30, 2008.

**Table of Contents****REGENERON PHARMACEUTICALS, INC.****Notes to Condensed Financial Statements (Unaudited)***(Unless otherwise noted, dollars in thousands, except per share data)***6. Accounts Receivable**

Accounts receivable as of September 30, 2008 and December 31, 2007 consist of the following:

	September 30, 2008	December 31, 2007
Receivable from the sanofi-aventis Group	\$ 37,744	\$ 14,244
Receivable from Bayer HealthCare	1,619	2,797
Other	2,843	1,279
	\$ 42,206	\$ 18,320

**7. Accounts Payable and Accrued Expenses**

Accounts payable and accrued expenses as of September 30, 2008 and December 31, 2007 consist of the following:

	September 30, 2008	December 31, 2007
Accounts payable	\$ 13,188	\$ 8,128
Payable to Bayer HealthCare		4,892
Accrued payroll and related costs	13,170	14,514
Accrued clinical trial expense	6,288	5,609
Accrued expenses, other	6,279	3,797
Interest payable on convertible notes	2,962	2,292
	\$ 41,887	\$ 39,232

**8. Repurchases of Convertible Debt**

During the first nine months of 2008, the Company repurchased a total of \$82.5 million in principal amount of its 5.5% Convertible Senior Subordinated Notes due October 17, 2008 (the Notes) for \$83.3 million. In connection with the repurchases of the Notes, the Company recognized a \$0.9 million loss on early extinguishment of debt, representing the premium paid on the Notes plus related unamortized debt issuance costs. At September 30, 2008, \$117.5 million of the Notes remained outstanding. Subsequently, such remaining outstanding Notes were repaid in full upon their maturity in October 2008.

**9. 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

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income taxes on comprehensive loss is immaterial. For the three and nine months ended September 30, 2008 and 2007, the components of comprehensive loss are:

	Three months ended September 30,	
	2008	2007
Net loss	\$ (21,115)	\$ (35,838)
Change in net unrealized gain (loss) on marketable securities	(3,645)	511
Total comprehensive loss	\$ (24,760)	\$ (35,327)

	Nine months ended September 30,	
	2008	2007
Net loss	\$ (51,192)	\$ (92,529)
Change in net unrealized gain (loss) on marketable securities	(4,130)	226
Total comprehensive loss	\$ (55,322)	\$ (92,303)

**10. License Agreement with Cellectis**

In July 2008, the Company and Cellectis S.A. ( Cellectis ) entered into an Amended and Restated Non-Exclusive License Agreement (the License Agreement ). The License Agreement resolves a dispute between the parties related to the interpretation of a license agreement entered into by the parties in December 2003 pursuant to which the Company licensed certain patents and patent applications from Cellectis. Pursuant to the License Agreement, in July 2008, the Company made a non-refundable \$12.5 million payment to Cellectis (the License Payment ) and agreed to pay Cellectis a low single-digit royalty based on revenue received by the Company from any future licenses or sales of the Company s *VelociGene*® or *VelocImmune*® products and services. No royalties are payable with respect to the Company s *VelocImmune* license agreements with AstraZeneca UK Limited ( AstraZeneca ) and Astellas Pharma Inc. ( Astellas ) or the Company s November 2007 collaboration with sanofi-aventis. Moreover, no royalties are payable on any revenue from commercial sales of antibodies from the Company s *VelocImmune* technology.

The Company began amortizing the License Payment in the second quarter of 2008 in proportion to past and future anticipated revenues under the Company s license agreements with AstraZeneca and Astellas and the Discovery and Preclinical Development Agreement under the Company s November 2007 collaboration with sanofi-aventis. During the three and nine months ended September 30, 2008, the Company recognized \$0.5 million and \$2.2 million, respectively, of expense in connection with the License Payment.

In July 2008, the Company and Cellectis also entered into a Subscription Agreement pursuant to which the Company has agreed to purchase 368,301 ordinary shares of Cellectis at a price of EUR 8.63 per share (which is equivalent to \$12.15 at the September 30<sup>th</sup> EUR exchange rate). The purchase was contingent upon approval by the board of directors of Cellectis and by

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**REGENERON PHARMACEUTICALS, INC.**

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

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

the shareholders of Collectis. Such approval was obtained on October 30, 2008, and the Company's purchase of the Collectis shares will be completed in early November 2008.

**11. VelociGene® Agreement with the sanofi-aventis Group**

In connection with the Company's November 2007 global strategic collaboration with sanofi-aventis to discover, develop, and commercialize fully human monoclonal antibodies, in August 2008, the Company entered into a separate agreement with sanofi-aventis to use Regeneron's proprietary *VelociGene* technology platform to supply sanofi-aventis with genetically modified mammalian models of gene function and disease. The agreement provides for minimum annual order quantities for the term of the agreement which extends through December 2012, for which Regeneron expects to receive payments totaling a minimum of \$21.5 million. This aggregate minimum amount is being recognized as contract research and development revenue in accordance with SAB 104 and Emerging Issues Task Force Issue No. 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables* (EITF 00-21). For the three and nine months ended September 30, 2008, the Company recognized \$0.5 million in revenue related to this agreement.

**12. Income Taxes**

During the quarter ended September 30, 2008, the Company implemented a tax planning strategy to utilize net operating loss carry-forwards (which were otherwise due to expire in 2008 through 2012) on its 2007 U.S. Federal and New York State income tax returns that were filed in the third quarter of 2008. The tax planning strategy included electing, for tax purposes only, to capitalize \$142.1 million of 2007 research and development (R&D) costs and to amortize these costs over ten years for tax purposes. By capitalizing these R&D costs, the Company was able to generate taxable income in 2007 and utilize the net operating loss carry-forwards to offset this taxable income. As a result, the Company incurred income tax expense of \$3.1 million for the three and nine months ended September 30, 2008, which relates to U.S. Federal and New York State alternative minimum tax (AMT) and includes \$0.2 million of interest and penalties.

The Company is primarily subject to U.S. Federal and New York State income tax. The Company's effective income tax rate is generally 0%. The difference between the Company's effective income tax rate and the Federal statutory rate of 35% is attributable to the use of net operating loss carry-forwards as well as state tax benefits and tax credit carry-forwards offset by changes in the deferred tax valuation allowance and the AMT discussed above.

**13. Amendment to Operating Lease Tarrytown, New York facilities**

The Company leases laboratory and office facilities in Tarrytown, New York. The Company entered into a new agreement in December 2006 (which was amended in October 2007) to lease laboratory and office space that is now under construction and expected to be completed in mid-2009 at the Company's current Tarrytown location, plus retain a portion of the Company's

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**REGENERON PHARMACEUTICALS, INC.**

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

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

existing space. In September 2008, the Company amended the operating lease agreement to increase the amount of existing space that the Company will retain under the lease. The term of the lease commenced effective June 2008 and will expire in June 2024. Other terms and conditions, as previously described in the Company's Annual Report on Form 10-K for the year ended December 31, 2007, remain unchanged.

In connection with the September 2008 operating lease amendment, the Company's total estimated future minimum noncancelable lease commitments under operating leases, previously disclosed in the Company's Annual Report on Form 10-K for the year ended December 31, 2007 will increase to \$10.2 million, \$17.3 million, \$17.4 million, and \$17.7 million for the years ended December 31, 2009, 2010, 2011, and 2012, respectively, and increase to \$230.3 million, in the aggregate, for years subsequent to 2012.

**14. Legal Matters**

From time to time, the Company is a party to legal proceedings in the course of its business. The Company does not expect any such current legal proceedings to have a material adverse effect on the Company's business or financial condition.

**15. 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.

In March 2008, the FASB issued SFAS 161, *Disclosures about Derivative Instruments and Hedging Activities* an Amendment of FASB Statement 133. SFAS 161 enhances required disclosures regarding derivatives and hedging activities, including enhanced disclosures regarding how (a) an entity uses derivative instruments, (b) derivative instruments and related hedged items are accounted for under SFAS 133, *Accounting for Derivative Instruments and Hedging Activities*, and (c) derivative instruments and related hedged items affect an entity's financial position, financial performance, and cash flows. SFAS 161 is effective for fiscal years and interim periods beginning after November 15, 2008. The Company is required to adopt SFAS 161 for the fiscal year beginning January 1, 2009. Management does not anticipate that the adoption of SFAS 161 will have a material impact on the Company's financial statements.

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**REGENERON PHARMACEUTICALS, INC.**

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

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

In April 2008, the FASB issued FASB Staff Position ( FSP ) FAS 142-3, *Determination of the Useful Life of Intangible Assets*. This FSP amends the factors that should be considered in developing renewal or extension assumptions used to determine the useful life of a recognized intangible asset under SFAS 142, *Goodwill and Other Intangible Assets*. The intent of this FSP is to improve the consistency between the useful life of a recognized intangible asset under SFAS 142 and the period of expected cash flows used to measure the fair value of the asset under SFAS 141R, and other generally accepted accounting principles ( GAAP ). This FSP is effective for fiscal years beginning after December 15, 2008. Early adoption is prohibited. The Company is required to adopt FSP FAS 142-3 for the fiscal year beginning January 1, 2009. Management does not anticipate that the adoption of this FSP will have a material impact on the Company's financial statements.

In May 2008, the FASB issued SFAS 162, *The Hierarchy of Generally Accepted Accounting Principles*. SFAS 162 identifies the sources of accounting principles and the framework for selecting the principles used in the preparation of financial statements of nongovernmental entities that are presented in conformity with GAAP in the United States. Any effect of applying the provisions of SFAS 162 shall be reported as a change in accounting principle in accordance with SFAS 154, *Accounting Changes and Error Corrections*. SFAS 162 is effective November 15, 2008. Management does not anticipate that the adoption of SFAS 162 will have a material impact on the Company's financial statements.

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**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® (rilonacept) Injection for Subcutaneous Use, which 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 three 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, VEGF Trap-Eye, which is being developed in eye diseases using intraocular delivery in collaboration with Bayer HealthCare LLC, and ARCALYST® (rilonacept; also known as IL-1 Trap) which will enter Phase 3 studies in the first half of 2009 both for the prevention of gout flares induced by the initiation of urate-lowering drug therapy used to control gout and in acute 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 is in a Phase 1 clinical trial in rheumatoid arthritis.

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 primarily 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.

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. However, developing and commercializing new medicines entails significant risk and expense.

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We believe that our ability to develop product candidates is enhanced by the application of our technology platforms. Our discovery platforms are designed to identify specific genes of therapeutic interest for a particular disease or cell type and validate targets through high-throughput production of mammalian models. Our human monoclonal antibody 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 the fourth quarter of 2007. We plan to file an Investigational New Drug Application (IND) for an antibody to Delta-like ligand-4 (Dl14) by the end of 2008. We plan to file an IND for a third antibody product candidate shortly thereafter, and to advance an average of two to three antibody product candidates into clinical development each year. We continue to invest in the development of enabling technologies to assist in our efforts to identify, develop, and commercialize new product candidates.

**Commercial Product:*****ARCALYST<sup>®</sup> (rilonacept) Cryopyrin-Associated Periodic Syndromes (CAPS)***

In February 2008, we received marketing approval from the U.S. Food and Drug Administration (FDA) for ARCALYST<sup>®</sup> (rilonacept) 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 March 2008, ARCALYST became available for prescription in the United States and we began making shipments to our distributors and transitioning the patients who participated in the CAPS pivotal study from clinical study drug to commercial supplies. This transition has been mostly completed and we currently project shipments of ARCALYST to our distributors to total approximately \$10 million in 2008. During the third quarter and first nine months of 2008, we shipped \$4.3 million and \$6.7 million, respectively, of ARCALYST to our distributors. In July 2008, we submitted a Marketing Authorization Application (MAA) to the European Medicines Agency (EMA) for ARCALYST for the treatment of CAPS in the European Union.

ARCALYST is a protein-based product designed to bind the interleukin-1 (called IL-1) cytokine and prevent its interaction with cell surface receptors. ARCALYST is the only therapy approved in the United States for patients with CAPS, a group of rare, inherited, auto-inflammatory conditions characterized by life-long, recurrent symptoms of rash, fever/chills, joint pain, eye redness/pain, and fatigue. Intermittent, disruptive exacerbations or flares can be triggered at any time by exposure to cooling temperatures, stress, exercise, or other unknown stimuli. CAPS is caused by a range of mutations in the gene NLRP3 (formerly known as *CIAS1*) which encodes a protein named cryopyrin. In addition to FCAS and MWS, CAPS includes Neonatal Onset Multisystem Inflammatory Disease (NOMID). ARCALYST has not been studied for the treatment of NOMID.



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### **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 (a process known as angiogenesis) 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 currently are enrolling patients in four Phase 3 trials that combine aflibercept with standard chemotherapy regimens. One trial is evaluating aflibercept as a 2<sup>nd</sup> line treatment for metastatic colorectal cancer (the VELOUR study) in combination with FOLFIRI (folinic acid (leucovorin), 5-fluorouracil, and irinotecan). A second trial is evaluating aflibercept as a 1<sup>st</sup> line treatment for metastatic pancreatic cancer in combination with gemcitabine (the VANILLA study). A third trial is evaluating aflibercept as a 1<sup>st</sup> line treatment for metastatic androgen independent prostate cancer in combination with docetaxel/prednisone (the VENICE study). The fourth trial is evaluating aflibercept as a 2<sup>nd</sup> line treatment for metastatic non-small cell lung cancer in combination with docetaxel (the VITAL study). All four trials are studying the current standard of chemotherapy care for the cancer being studied with and without aflibercept. In addition, a Phase 2 study of aflibercept in 1st-line metastatic colorectal cancer in combination with folinic acid (leucovorin), 5-fluorouracil, and oxaliplatin is expected to begin by the end of 2008.

Aflibercept is also being studied in a Phase 2 single-agent study in advanced ovarian cancer (AOC) patients with symptomatic malignant ascites (SMA). This trial is more than 90% enrolled and patients continue to be enrolled in the study. A separate non-blinded single-agent aflibercept study in 16 AOC patients with SMA has been completed and the results are currently being evaluated. In 2004, the FDA granted Fast Track designation to aflibercept for the treatment of SMA.

Sanofi-aventis has also expanded the aflibercept development program to Japan, where they are conducting Phase 1 safety and tolerability studies in combination with standard chemotherapies in patients with advanced solid malignancies.

In addition, multiple exploratory studies are currently underway or scheduled to begin that are being or will be 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. At the 2008 annual meeting of the American Society of Clinical Oncology (ASCO), investigators reported preliminary results of an NCI-sponsored study of single-agent aflibercept in 48 patients with either relapsed or first recurrence temozolomide-resistant glioblastoma multiforme or anaplastic glioma. As assessed by the investigators, responses were achieved in 50% of patients with anaplastic glioma

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and 30% of patients with glioblastoma. As assessed by an independent radiological reading center, preliminary data indicates that responses were achieved in approximately 30% of patients with anaplastic glioma and 22% of patients with glioblastoma. Grade 3 adverse events in this study included fatigue, hypertension, hand-foot syndrome, lymphopenia, thrombosis, and proteinuria.

In September 2008, at the 2008 ASCO Breast Cancer Symposium, investigators reported the results of a small, exploratory NCI-sponsored study in 21 patients with poor prognostic characteristics (i.e., tumors resistant to anthracyclines and/or taxanes and a majority with metastatic visceral disease). In this trial, single-agent aflibercept had a confirmed partial response rate, as assessed by the investigators, of 5% (with a 95% Confidence Interval of 0-24%), a median progression free survival (PFS) of 2.7 months, and a median overall survival (OS) of 10.8 months. There were no unexpected safety concerns in this small study. The investigators reported that there were two cases of congestive heart failure in patients at high risk.

### **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 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

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neovascular form of Age-related Macular Degeneration (wet AMD). We and Bayer HealthCare are also developing VEGF Trap-Eye in diabetic macular edema (DME) and plan to initiate a Phase 2 study in patients with DME in early 2009.

The Phase 3 trials in wet AMD, known as VIEW 1 and VIEW 2 (VEGF Trap: Investigation of Efficacy and Safety in Wet age-related macular degeneration), are comparing VEGF Trap-Eye and ranibizumab (Lucentis®, a registered trademark of Genetech, Inc.), an anti-angiogenic agent approved for use in wet AMD. VIEW 1 is being conducted in North America and VIEW 2 is being conducted in Europe, Asia Pacific, Japan and Latin America. The VIEW 1 and VIEW 2 trials are both evaluating dosing intervals of four and eight weeks for VEGF Trap-Eye compared with ranibizumab dosed according to its U.S. label every four weeks over the first year. As needed dosing (PRN) with both agents will be evaluated in the second year of the studies.

In August 2008, we and Bayer HealthCare AG announced the preliminary results of a Phase 2 study in wet AMD which demonstrated that patients treated with the VEGF Trap-Eye achieved durable improvements in visual acuity and retinal thickness for up to one year in wet AMD. In September 2008, the complete results of this study, including additional data on reductions in the active choroidal neovascularization lesion size, were reported at the 2008 annual meeting of the Retina Society in Scottsdale, Arizona.

In this double-masked Phase 2 trial, patients were initially treated with either fixed monthly or quarterly dosing for 12 weeks and then continued to receive treatment for another 40 weeks on a PRN dosing schedule. Patients receiving monthly doses of VEGF Trap-Eye of either 2.0 or 0.5 milligrams (mg) for 12 weeks followed by PRN dosing achieved mean improvements in visual acuity versus baseline of 9.0 letters ( $p < 0.0001$  versus baseline) and 5.4 letters ( $p < 0.085$  versus baseline), respectively, at the end of one year. The proportion of patients with vision of 20/40 or better (part of the legal minimum requirement for an unrestricted driver's license in the U.S.) increased from 23% at baseline to 45% at week 52 in patients initially treated with 2.0 mg monthly and from 16% at baseline to 47% at week 52 in patients initially treated with 0.5 mg monthly.

Patients receiving monthly doses of VEGF Trap-Eye of either 2.0 or 0.5 mg for 12 weeks followed by PRN dosing also achieved mean decreases in retinal thickness versus baseline of 143 microns ( $p < 0.0001$  versus baseline) and 125 microns ( $p < 0.0001$  versus baseline) at week 52, respectively.

During the week 12 to week 52 PRN dosing period, patients initially dosed on a 2.0 mg monthly schedule received, on average, only 1.6 additional injections and those initially dosed on a 0.5 mg monthly schedule received, on average, 2.5 additional injections.

While PRN dosing following a fixed quarterly dosing regimen (with dosing at baseline and week 12) also yielded improvements in visual acuity and retinal thickness versus baseline at week 52, the results generally were not as robust as those obtained with initial fixed monthly dosing.

In this Phase 2 study, treatment with VEGF Trap-Eye was also associated with a reduction in the size of the total active choroidal neovascular membrane (CNV), the active lesion that is the

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underlying cause of vision loss in patients with wet AMD. Patients initially receiving either a 2.0 mg or 0.5 mg monthly fixed dose of VEGF Trap-Eye for 12 weeks followed by PRN dosing experienced statistically significant 3.41 mm<sup>2</sup> and 1.42 mm<sup>2</sup> reductions in mean CNV size at 48 weeks (the final one-year analysis endpoint from the independent reading center) versus baseline, respectively. Patients in the 2.0 mg monthly cohort also achieved a statistically significant 1.75 mm<sup>2</sup> reduction in total lesion size. A reduction in total lesion size was not seen in the cohort initially dosed with 0.5 mg monthly.

VEGF Trap-Eye was generally 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 commonly reported adverse events were those typically associated with intravitreal injections.

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. Wet AMD and diabetic retinopathy (which includes DME) 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 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.

**3. ARCALYST® (rilonacept) *Inflammatory Diseases***

We are evaluating ARCALYST in a number of diseases and disorders, in addition to CAPS, where IL-1 may play an important role. In September 2008, we announced the results of a Phase 2 study which evaluated the efficacy and safety of ARCALYST versus placebo in the prevention of gout flares induced by the initiation of urate-lowering drug therapy that is used to control

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gout. In this 83-patient, double-blind, placebo-controlled study, the mean number of flares per patient over the first 12 weeks of urate-lowering therapy was 0.79 with placebo and 0.15 with rilonacept ( $p=0.0011$ ), an 81% reduction. This was the primary endpoint of the study. All secondary endpoints also were met with statistical significance.

In the first 12 weeks of treatment, 45.2% of patients treated with placebo experienced a gout flare and, of those, 47.4% had more than one flare. Among patients treated with ARCALYST® (rilonacept), only 14.6% experienced a gout flare ( $p=0.0037$  versus placebo) and none had more than one flare. Injection-site reaction was the most commonly reported adverse event with ARCALYST treatment and no serious drug-related adverse events were reported.

Gout is characterized by high blood levels of uric acid, a bodily waste product normally excreted by the kidneys. The uric acid can form crystals in the joints of the toes, ankles, knees, wrists, fingers, and elbows. Chronic treatment with uric acid-lowering medicines, such as allopurinol, is prescribed to eliminate the uric acid crystals and prevent reformation. During the first months of allopurinol therapy, while uric acid blood levels are being reduced, the break up of the uric acid crystals can result in stimulation of inflammatory mediators, including IL-1, resulting in acute flares of joint pain and inflammation. These painful flares generally persist for at least five days.

We plan to initiate a Phase 3 clinical development program with ARCALYST in the first half of 2009 both for the prevention of gout flares in patients initiating urate-lowering drug therapy and in acute gout. We are also planning to evaluate ARCALYST in other indications in which IL-1 may play a role.

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.

### **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

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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 exploiting our *VelociGene®* technology platform (see below), in a process in which six megabases of mouse immune gene loci were replaced, or humanized, with corresponding human immune gene loci. The *VelocImmune* mice can be used to generate efficiently fully human monoclonal antibodies to targets of therapeutic interest. *VelocImmune* and our related technologies offer the potential to increase the speed and efficiency through which human monoclonal antibody therapeutics may be discovered and validated, thereby improving the overall efficiency of our early stage drug development activities. We are utilizing the *VelocImmune* technology to produce our next generation of drug candidates for preclinical development, and are exploring possible 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 is REGN88, an antibody to the interleukin-6 receptor (IL-6R), that is being evaluated in rheumatoid arthritis. The second is expected to be an antibody to Delta-like ligand-4 (Dl14), for which we plan to file an IND by the end of 2008. We plan to file an IND for a third therapeutic antibody shortly thereafter and to advance an average of two to three antibody candidates into clinical development each year.

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

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million from sanofi-aventis under the discovery agreement. In addition, sanofi-aventis is funding 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*<sup>®</sup> technology in its internal research 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 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 two \$20.0 million non-refundable payments to us, one in April 2007 and the other in June 2008. Astellas is required to make up to four 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 Astellas using our *VelocImmune* technology.

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### **Academic *VelocImmune*<sup>®</sup> Investigators Program**

In September 2008, we entered into an agreement that will provide researchers at Columbia University Medical Center with access to our *VelocImmune* technology platform. Under the agreement, scientists at Columbia will use *VelocImmune* mice to generate antibodies against their research targets and will conduct research to discover potential human therapeutics based on the antibodies. We have an exclusive option to license the antibodies for development and commercialization as therapeutic or diagnostic products and will pay Columbia a low single-digit royalty on ensuing product sales.

### ***VelociGene*<sup>®</sup> 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.

In August 2008, we entered into a separate agreement with sanofi-aventis to use our *VelociGene* platform to supply sanofi-aventis with genetically modified mammalian models of gene function and disease. Sanofi-aventis will pay us a minimum of \$21.5 million for the term of the agreement, which extends through December 2012, for knock-out and transgenic models of gene function for target genes identified by sanofi-aventis. Sanofi-aventis will use these models for its internal research programs, outside of the scope of the antibody collaboration between us and sanofi-aventis.

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 of research institutions, the other major participants in the Knockout Mouse Project, to use



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components of our *VelociGene*<sup>®</sup> 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, as amended in September 2008, we are entitled to receive a minimum of \$24.5 million over a five-year period, including \$1.5 million to optimize our existing C57BL/6 ES cell line and its proprietary growth medium, both of which are being 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 rapid generation of expression cell lines for our Traps and our *VelocImmune*<sup>®</sup> 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 September 30, 2008, we had a cumulative loss of \$844.4 million. As described above, in February 2008, we received FDA approval for ARCALYST<sup>®</sup> (rilonacept) 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 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.

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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:

<b>Clinical Program</b>	<b>2008 Events to Date</b>	<b>2008-9 Plans (next 12 months)</b>
ARCALYST® (rilonacept; also known as IL-1 Trap)	Received FDA approval for CAPS Launched ARCALYST commercially in CAPS Reported data from a Phase 2 study in the prevention of gout flares in patients initiating urate-lowering drug therapy	Initiate Phase 3 development program of ARCALYST in the prevention of gout flares in patients initiating urate-lowering drug therapy and in acute gout Evaluate ARCALYST in other disease indications in which IL-1 may play a role
Aflibercept (VEGF Trap Oncology)	Reported final data from Phase 2 single-agent trial in advanced ovarian cancer Reported results from four Phase 1 dose-escalation studies in combination with chemotherapy in solid tumors	Sanofi-aventis to initiate Phase 2 1st-line study in metastatic colorectal cancer in combination with a standard chemotherapy regimen Complete enrollment of Phase 2 single-agent study in symptomatic malignant ascites (SMA) and report results Sanofi-aventis to continue enrollment of four Phase 3 studies
VEGF Trap-Eye (intravitreal injection)	Presented positive final data through 52 weeks from the Phase 2 trial in wet AMD Bayer HealthCare initiated second Phase 3 trial (VIEW 2) in wet AMD outside the United States	Initiate a Phase 2 clinical study in DME Continue enrolling patients in VIEW 1 and VIEW 2 trials
Antibodies	Finalized preparations for initiation of clinical program for the Dll4 antibody	Initiate Phase 1 trial for the Dll4 antibody in oncology Report data from Phase 1 trial of REGN88 in rheumatoid arthritis Advance additional antibody candidate(s) into clinical development

**ARCALYST® (rilonacept) Product Revenue and Inventory*****Product Revenue***

In March 2008, ARCALYST became available for prescription in the United States for the treatment of CAPS. We currently expect shipments of ARCALYST to our distributors to total approximately \$10 million in 2008.

We 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

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passed to the customer, the price is fixed or determinable, collection from the customer is reasonably assured and we have no further performance obligations. Revenues from product sales are recorded net of applicable provisions for prompt pay discounts, product returns, and estimated rebates payable under governmental programs (including Medicaid), distributor fees, and other sales-related costs. 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. We review our estimates of rebates payable each period and record any necessary adjustments in the current period's net product sales.

During the three and nine months ended September 30, 2008, we recognized as revenue \$2.7 million of ARCALYST<sup>®</sup> (rilonacept) net product sales for which both the right of return no longer exists and rebates can be reasonably estimated. At September 30, 2008, deferred revenue related to ARCALYST net product sales totaled \$3.8 million.

### ***Inventory***

We began capitalizing inventory costs associated with commercial supplies of ARCALYST subsequent to receipt of marketing approval from the FDA in February 2008. Costs for manufacturing supplies of ARCALYST prior to receipt of FDA approval were recognized as research and development expenses in the period that the costs were incurred. Therefore, these costs are not being included in cost of goods sold when revenue is recognized from the sale of those supplies of ARCALYST. For the three and nine months ended September 30, 2008, ARCALYST cost of goods sold totaled \$0.3 million. At September 30, 2008, inventoried costs related to ARCALYST were insignificant.

### ***Velocigene<sup>®</sup> Agreement with the sanofi-aventis Group***

In connection with our November 2007 global strategic collaboration with sanofi-aventis to discover, develop, and commercialize fully human monoclonal antibodies, in August 2008, we entered into a separate agreement with sanofi-aventis to use our proprietary *VelociGene* technology platform to supply sanofi-aventis with genetically modified mammalian models of gene function and disease. The agreement provides for minimum annual order quantities for the term of the agreement which extends through December 2012, for which we expect to receive payments totaling a minimum of \$21.5 million. This aggregate minimum amount is being recognized as contract research and development revenue in accordance with SAB 104 and Emerging Issues Task Force Issue No. 00-21, *Accounting for Revenue Arrangements with Multiple Deliverables* (EITF 00-21). For the three and nine months ended September 30, 2008, we recognized \$0.5 million in revenue related to this agreement.

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

In July 2008, we and Collectis S.A. entered into an Amended and Restated Non-Exclusive License Agreement. The amended license agreement resolves a dispute between the parties related to the interpretation of a license agreement entered into by the parties in December 2003 pursuant to which we licensed certain patents and patent applications relating to a process for the

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specific replacement of a copy of a gene in the receiver genome by homologous recombination. Pursuant to the amended license agreement, in July 2008, we made a non-refundable \$12.5 million payment to Collectis and agreed to pay Collectis a low single-digit royalty based on revenue received by us from any future licenses or sales of our *VelociGene*<sup>®</sup> or *VelocImmune*<sup>®</sup> products and services. No royalties are payable with respect to our *VelocImmune* license agreements with AstraZeneca and Astellas or our November 2007 collaboration with sanofi-aventis. Moreover, no royalties are payable on any revenue from commercial sales of antibodies from our *VelocImmune* technology.

We began amortizing our \$12.5 million payment to Collectis in the second quarter of 2008 in proportion to past and anticipated future revenues under our license agreements with AstraZeneca and Astellas and our antibody discovery agreement with sanofi-aventis. During the three and nine months ended September 30, 2008, the Company recognized \$0.5 million and \$2.2 million of expense related to this agreement.

In July 2008, we and Collectis also entered into a Subscription Agreement pursuant to which we agreed to purchase 368,301 ordinary shares of Collectis at a price of EUR 8.63 per share. The purchase was contingent upon approval by the board of directors of Collectis and by the shareholders of Collectis. Such approval was obtained on October 30, 2008, and our purchase of the Collectis shares will be completed in early November 2008.

**Results of Operations**

***Three Months Ended September 30, 2008 and 2007***

***Net Loss:***

Regeneron reported a net loss of \$21.1 million, or \$0.27 per share (basic and diluted), for the third quarter of 2008 compared to a net loss of \$35.8 million, or \$0.54 per share (basic and diluted), for the third quarter of 2007. The decrease in net loss was principally due to revenues earned in the third 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.

**Table of Contents***Revenues:*

Revenues for the three months ended September 30, 2008 and 2007 consist of the following:

<i>(In millions)</i>	<b>2008</b>	<b>2007</b>
Contract research & development revenue		
Sanofi-aventis	\$ 42.0	\$ 9.2
Bayer HealthCare	9.0	
Other	1.9	3.1
Total contract research & development revenue	52.9	12.3
Technology licensing revenue	10.0	10.0
Net product sales of ARCALYST® (rilonacept)	2.7	
Total revenue	\$ 65.6	\$ 22.3

We recognize revenue from sanofi-aventis, in connection with our aflibercept and antibody collaborations in accordance with SAB 104 and EITF 00-21. Contract research and development revenue from sanofi-aventis, as detailed below, consists primarily of reimbursement for research and development expenses and recognition of revenue related to non-refundable, up-front payments of \$105.0 million related to the 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.

	<b>Three months ended September 30,</b>	
<b>Sanofi-aventis Contract Research &amp; Development Revenue</b>	<b>2008</b>	<b>2007</b>
<i>(In millions)</i>		
Aflibercept:		
Regeneron expense reimbursement	\$ 7.3	\$ 7.0
Recognition of deferred revenue related to up-front payments	2.1	2.2
Total aflibercept	9.4	9.2
Antibody:		
Regeneron expense reimbursement	29.5	
Recognition of deferred revenue related to up-front payment	2.6	
Recognition of revenue related to <i>VelociGene</i> ® agreement	0.5	
Total antibody	32.6	
Total sanofi-aventis contract research & development revenue	\$ 42.0	\$ 9.2

Sanofi-aventis reimbursement of Regeneron's aflibercept expenses increased in the third quarter of 2008 compared to the same period in 2007, primarily due to higher clinical development costs and higher costs related to manufacturing aflibercept clinical supplies. Recognition of deferred revenue related to sanofi-aventis up-front aflibercept payments decreased in the third 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 September 30, 2008, \$54.9 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 third quarter of 2008, sanofi-aventis reimbursement of Regeneron's antibody expenses consisted of \$24.1 million under the discovery agreement and \$5.4 million of development costs related to REGN88 under the license agreement. Recognition of deferred revenue under the antibody collaboration related to sanofi-aventis \$85.0 million up-front payment. As of September 30, 2008, \$76.2 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 third 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 payment and the \$20.0 million milestone payment, and (ii) \$5.7 million related to the portion of our third quarter 2008 VEGF Trap-Eye development expenses that is reimbursable from Bayer HealthCare. As of September 30, 2008, \$69.2 million of the up-front and milestone payments was deferred and will be recognized as revenue in future periods.

Other contract research and development revenue includes \$1.2 million and \$2.2 million, respectively, recognized in the third quarters 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 *VelocImmune*<sup>®</sup> license agreements with AstraZeneca and Astellas, each of the \$20.0 million annual non-refundable payments is deferred upon receipt and recognized as revenue ratably over approximately the ensuing year of each agreement. In both the third quarter of 2008 and 2007 we recognized \$10.0 million of technology licensing revenue related to these agreements.

As described above, during the three months ended September 30, 2008, we recognized as revenue \$2.7 million of ARCALYST<sup>®</sup> (rilonacept) net product sales.

**Table of Contents***Expenses:*

Total operating expenses increased to \$85.5 million in the third quarter of 2008 from \$61.0 million in the same period of 2007. Our average headcount increased to 851 in the third quarter of 2008 from 639 in the same period of 2007 primarily as a result of the Company's expanding research and development activities which are primarily attributable to the Company's antibody collaboration with sanofi-aventis.

Operating expenses in the third quarter of 2008 and 2007 include a total of \$8.2 million and \$7.0 million, respectively, of non-cash compensation expense related to employee stock option and restricted stock awards (Non-cash Compensation Expense), as detailed below:

Expenses (In millions)	For the three months ended September 30, 2008		
	Expenses before inclusion of		Expenses as Reported
	Non-cash	Non-cash	
	Compensation Expense	Compensation Expense	
Research and development	\$ 68.8	\$ 5.0	\$ 73.8
Selling, general, and administrative	8.2	3.2	11.4
Cost of goods sold	0.3		0.3
Total operating expenses	\$ 77.3	\$ 8.2	\$ 85.5

Expenses (In millions)	For the three months ended September 30, 2007		
	Expenses before inclusion of		Expenses as Reported
	Non-cash	Non-cash	
	Compensation Expense	Compensation Expense	
Research and development	\$ 47.6	\$ 4.1	\$ 51.7
Selling, general, and administrative	6.4	2.9	9.3
Total operating expenses	\$ 54.0	\$ 7.0	\$ 61.0

*Research and Development Expenses:*

Research and development expenses increased to \$73.8 million in the third quarter of 2008 from \$51.7 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 September 30, 2008 and 2007:



	For the three months ended September 30,		
	2008	2007	Increase (Decrease)
<b>Research and development expenses</b> <i>(In millions)</i>			
Payroll and benefits (1)	\$ 22.5	\$ 15.2	\$ 7.3
Clinical trial expenses	14.7	12.9	1.8
Clinical manufacturing costs (2)	13.8	11.9	1.9
Research and preclinical development costs	8.7	5.8	2.9
Occupancy and other operating costs	10.5	5.9	4.6
Cost-sharing of Bayer HealthCare VEGF Trap-Eye development expenses (3)	3.6		3.6
Total research and development expenses	\$ 73.8	\$ 51.7	\$ 22.1

(1) Includes \$4.3 million and \$3.4 million of Non-cash Compensation Expense for the three months ended September 30, 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 September 30, 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 its VEGF Trap-Eye development expenses that we are obligated to reimburse. Bayer HealthCare provides us with estimated VEGF Trap-Eye development expenses for the most recent interim fiscal quarter. Bayer HealthCare's estimate is reconciled to its actual expenses for such quarter in the subsequent interim quarter and our portion of its VEGF Trap-Eye development expenses that we are obligated to reimburse is adjusted accordingly. 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 clinical development programs for (i) ARCALYST, which includes our Phase 2 gout flare prevention clinical study, (ii) monoclonal antibodies, which includes REGN88 as well as clinical-related preparatory activities for the Dll4 antibody, and (iii) VEGF Trap-Eye, which includes our VIEW 1 trial in wet AMD. Clinical manufacturing costs increased due primarily to higher expenses related to VEGF Trap-Eye and monoclonal antibodies, including REGN88. These increases were partially offset by a reduction in manufacturing costs associated with ARCALYST. Research and preclinical development costs increased primarily due to higher costs associated with our antibody programs. Occupancy and other operating costs

increased principally as a result of our higher headcount and 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 are shown below:

<b>Project Costs</b> <i>(In millions)</i>	<b>For the three months ended September 30,</b>		
	<b>2008</b>	<b>2007</b>	<b>Increase (Decrease)</b>
ARCALYST® (rilonacept)	\$ 9.7	\$ 12.9	\$ (3.2)
Aflibercept	6.6	5.5	1.1
VEGF Trap-Eye	18.7	14.1	4.6
REGN88	5.4		5.4
Other research programs & unallocated costs	33.4	19.2	14.2
Total research and development expenses	\$ 73.8	\$ 51.7	\$ 22.1

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

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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<sup>®</sup> (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<sup>®</sup> (rilonacept) 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 \$11.4 million in the third quarter of 2008 from \$9.3 million in the same period of 2007. In the third quarter of 2008, we incurred selling expenses of \$0.7 million related to ARCALYST for the treatment of CAPS. General and administrative expenses increased in the third quarter of 2008 due to (i) higher compensation expense due primarily to increases in administrative headcount to support our expanded research

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and development activities, (ii) higher recruitment and related costs associated with expanding our headcount, and (iii) higher administrative facility-related costs.

*Cost of goods sold:*

As described above, during the third quarter of 2008, we began recognizing revenue and cost of goods sold from net product sales of ARCALYST<sup>®</sup> (rilonacept). Cost of goods sold was \$0.3 million for the third quarter of 2008.

*Other Income and Expense:*

Investment income decreased to \$3.7 million in the third quarter of 2008 from \$5.8 million in the comparable quarter of 2007, due primarily to lower yields on our cash and marketable securities. In addition, during the third quarter of 2008, deterioration in the credit quality of a marketable security from one issuer subjected us to the risk of not being able to recover the security's \$2.0 million carrying value. As a result, we recognized a \$1.7 million charge related to this security, which we considered to be other than temporarily impaired, partially offset by realized gains of \$1.0 million on sales of marketable securities during the third quarter of 2008.

Interest expense of \$1.8 million and \$3.0 million in the third quarter of 2008 and 2007, respectively, is attributable to our 5.5% Convertible Senior Subordinated Notes due October 17, 2008. During the second and third quarters of 2008, we repurchased a total of \$82.5 million in principal amount of these convertible notes for \$83.3 million. At September 30, 2008, \$117.5 million of the convertible notes remained outstanding and were subsequently repaid in full upon their maturity in October 2008.

*Income Tax Expense:*

In the third quarter of 2008, we implemented a tax planning strategy which resulted in the utilization of certain net operating loss carry-forwards for tax purposes that would otherwise have expired over the next several years. As a result, we incurred income tax expense of \$3.1 million, which relates to U.S. Federal and New York State alternative minimum tax and includes \$0.2 million of interest and penalties.

***Nine Months Ended September 30, 2008 and 2007***

*Net Loss:*

We reported a net loss of \$51.2 million, or \$0.65 per share (basic and diluted), for the first nine months of 2008 compared to a net loss of \$92.5 million, or \$1.40 per share (basic and diluted), for the same period of 2007. The decrease in net loss was principally due to revenues earned in the first nine months of 2008 in connection with our antibody collaboration with sanofi-aventis and our VEGF Trap-Eye collaboration with Bayer HealthCare, partially offset by higher research and development expenses.

**Table of Contents***Revenues:*

Revenues for the nine months ended September 30, 2008 and 2007 consist of the following:

<i>(In millions)</i>	<b>2008</b>	<b>2007</b>
Contract research & development revenue		
Sanofi-aventis	\$ 116.3	\$ 34.5
Bayer HealthCare	28.2	
Other	5.4	7.4
Total contract research & development revenue	149.9	41.9
Technology licensing revenue	30.0	18.4
Net product sales of ARCALYST <sup>®</sup> (rilonacept)	2.7	
Total revenue	\$ 182.6	\$ 60.3

We recognize revenue from sanofi-aventis, in connection with our aflibercept and antibody collaborations in accordance with SAB 104 and EITF 00-21, as described above under Revenues, for the three months ended September 30, 2008 and 2007.

	<b>Nine months ended September 30,</b>	
	<b>2008</b>	<b>2007</b>
<b>Sanofi-aventis Contract Research &amp; Development Revenue</b>		
<i>(In millions)</i>		
Aflibercept:		
Regeneron expense reimbursement	\$ 29.3	\$ 27.8
Recognition of deferred revenue related to up-front payments	6.2	6.7
Total aflibercept	35.5	34.5
Antibody:		
Regeneron expense reimbursement	72.4	
Recognition of deferred revenue related to up-front payment	7.9	
Recognition of revenue related to <i>VelociGene</i> <sup>®</sup> agreement	0.5	
Total antibody	80.8	
Total sanofi-aventis contract research & development revenue	\$ 116.3	\$ 34.5

Sanofi-aventis reimbursement of our aflibercept expenses increased in the first nine months of 2008 compared to the same period in 2007, primarily due to higher clinical development costs and higher costs related to manufacturing aflibercept clinical supplies, partially offset by lower aflibercept preclinical development costs. Recognition of deferred revenue related to sanofi-aventis up-front aflibercept payments decreased in the first nine months 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.

In the first nine months of 2008, sanofi-aventis reimbursement of Regeneron's antibody expenses consisted of \$56.5 million under the discovery agreement and \$15.9 million of development costs related to REGN88, under the license agreement. Recognition of deferred revenue under the antibody collaboration related to sanofi-aventis \$85.0 million up-front payment.





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In the first nine months of 2008, we recognized contract research and development revenue of \$28.2 million from Bayer HealthCare, consisting of (i) \$9.9 million related to the \$75.0 million up-front payment and the \$20.0 million milestone payment, and (ii) \$18.3 million related to the portion of our VEGF Trap-Eye development expenses incurred in the first nine months of 2008 that is reimbursable from Bayer HealthCare.

Other contract research and development revenue includes \$3.6 million and \$4.5 million recognized in the first nine months of 2008 and 2007, respectively, 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 *VelocImmune*<sup>®</sup> 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 nine months of 2008 and 2007, we recognized \$30.0 million and \$18.4 million, respectively, of technology licensing revenue related to these agreements.

As described above, during the nine months ended September 30, 2008, we recognized as revenue \$2.7 million of ARCALYST<sup>®</sup> (rilonacept) net product sales.

**Expenses:**

Total operating expenses increased to \$237.9 million in the first nine months of 2008 from \$163.2 million in the same period of 2007. Our average headcount increased to 778 in the first nine months of 2008 from 614 in the same period of 2007 primarily as a result of the Company's expanding research and development activities which are primarily attributable to the Company's antibody collaboration with sanofi-aventis.

Operating expenses for the first nine months of 2008 and 2007 include a total of \$24.7 million and \$20.5 million, respectively, of Non-cash Compensation Expense, as detailed below:

<b>Expenses (In millions)</b>	<b>For the nine months ended September 30, 2008</b>		
	<b>Expenses before inclusion of Non-cash Compensation Expense</b>	<b>Non-cash Compensation Expense</b>	<b>Expenses as Reported</b>
Research and development	\$ 186.9	\$ 14.8	\$ 201.7
Selling, general, and administrative	26.0	9.9	35.9
Cost of goods sold	0.3		0.3
Total operating expenses	\$ 213.2	\$ 24.7	\$ 237.9

<b>Expenses (In millions)</b>	<b>For the nine months ended September 30, 2007</b>		
	<b>Expenses before inclusion of Non-cash Compensation Expense</b>	<b>Non-cash Compensation Expense</b>	<b>Expenses as Reported</b>
Research and development	\$ 124.8	\$ 12.0	\$ 136.8
Selling, general, and administrative	17.9	8.5	26.4

Total operating expenses	\$ 142.7	\$ 20.5	\$ 163.2
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**Table of Contents***Research and Development Expenses:*

Research and development expenses increased to \$201.7 million in the first nine months of 2008 from \$136.8 million in the same period of 2007. The following table summarizes the major categories of our research and development expenses for the nine months ended September 30, 2008 and 2007:

	<b>For the nine months ended September 30,</b>		
	<b>2008</b>	<b>2007</b>	<b>Increase (Decrease)</b>
<b>Research and development expenses</b>			
<i>(In millions)</i>			
Payroll and benefits (1)	\$ 61.4	\$ 43.3	\$ 18.1
Clinical trial expenses	35.2	24.8	10.4
Clinical manufacturing costs (2)	40.3	33.8	6.5
Research and preclinical development costs	21.6	17.9	3.7
Occupancy and other operating costs	24.2	17.0	7.2
Cost-sharing of Bayer HealthCare VEGF Trap-Eye development expenses (3)	19.0		19.0
Total research and development expenses	\$ 201.7	\$ 136.8	\$ 64.9

(1) Includes \$12.6 million and \$9.8 million of Non-cash Compensation Expense for the nine months ended September 30, 2008 and 2007, respectively.

(2) Represents the full cost of manufacturing drug for use in research, preclinical development, and clinical trials, including related payroll and benefits, Non-cash Compensation Expense, manufacturing materials and

supplies,  
depreciation,  
and occupancy  
costs of our  
Rensselaer  
manufacturing  
facility.

Includes  
\$2.2 million of  
Non-cash  
Compensation  
Expense for  
both the nine  
months ended  
September 30,  
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 its  
VEGF Trap-Eye  
development  
expenses that  
we are obligated  
to reimburse.  
Bayer  
HealthCare  
provides us with  
estimated VEGF  
Trap-Eye  
development  
expenses for the  
most recent  
interim fiscal  
quarter. Bayer  
HealthCare's  
estimate is

reconciled to its actual expenses for such quarter in the subsequent interim quarter and our portion of its VEGF Trap-Eye development expenses that we are obligated to reimburse is adjusted accordingly. 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 clinical development programs for (i) ARCALYST<sup>®</sup> (rilonacept), which includes our Phase 2 gout flare prevention clinical study, (ii) monoclonal antibodies, which includes REGN88 as well as clinical-related preparatory activities for the Dll4 antibody, and (iii) VEGF Trap-Eye, which includes our VIEW 1 trial in wet AMD. Clinical manufacturing costs increased due primarily to higher expenses related to VEGF Trap-Eye and monoclonal antibodies, including REGN88 and the Dll4 antibody. These increases were partially offset by a reduction in manufacturing costs associated with ARCALYST. Research and preclinical development costs increased primarily due to higher costs associated with our antibody programs. Occupancy and other operating costs increased principally as a result of our higher headcount and 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

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multiple projects. Our estimates of research and development costs for clinical development programs are shown below:

<b>Project Costs (In millions)</b>	<b>For the nine months ended September 30,</b>		
	<b>2008</b>	<b>2007</b>	<b>Increase (Decrease)</b>
ARCALYST® (rilonacept)	\$ 24.9	\$ 28.7	\$ (3.8)
Aflibercept	25.4	23.3	2.1
VEGF Trap-Eye	57.6	28.3	29.3
REGN88	14.7		14.7
Other research programs & unallocated costs	79.1	56.5	22.6
Total research and development expenses	\$ 201.7	\$ 136.8	\$ 64.9

For the reasons described above under **Research and Development Expenses** for the three months ended September 30, 2008 and 2007, 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 \$35.9 million in the first nine months of 2008 from \$26.4 million in the same period of 2007. In the first nine months of 2008, we incurred \$3.6 million of selling expenses related to ARCALYST for the treatment of CAPS. General and administrative expenses increased in the first nine months of 2008 due to (i) higher compensation expense due primarily to increases in administrative headcount to support our expanded research and development activities, (ii) higher recruitment and related costs associated with expanding our headcount, (iii) higher fees for professional services related to various general corporate matters, and (iv) higher administrative facility-related costs.

*Cost of Goods Sold:*

As described above, during the third quarter of 2008, we began recognizing revenue and cost of goods sold from net product sales of ARCALYST. Cost of goods sold was \$0.3 million for the first nine months of 2008.

*Other Income and Expense:*

Investment income decreased to \$15.5 million in the first nine months of 2008 from \$19.4 million in the same period of 2007, due primarily to lower yields on our cash and marketable securities. In addition, during the nine months ended September 30, 2008, deterioration in the credit quality of marketable securities from two issuers subjected us to the risk of not being able to recover the securities \$2.8 million carrying value. As a result, we recognized charges of \$2.3

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million related to these securities, which we considered to be other than temporarily impaired, partially offset by realized gains of \$1.1 million on sales of marketable securities during the first nine months of 2008.

Interest expense of \$7.5 million and \$9.0 million for the first nine months of 2008 and 2007, respectively, is attributable to our 5.5% Convertible Senior Subordinated Notes due October 17, 2008. In the first nine months of 2008, we repurchased a total of \$82.5 million in principal amount of these convertible notes for \$83.3 million. In connection with the repurchases, we recognized a \$0.9 million loss on early extinguishment of debt, representing the premium paid on the notes plus related unamortized debt issuance costs. At September 30, 2008, \$117.5 million of the convertible notes remained outstanding and were subsequently repaid in full upon their maturity in October 2008.

***Income Tax Expense***

In the third quarter of 2008, we implemented a tax planning strategy which resulted in the utilization of certain net operating loss carry-forwards for tax purposes that would otherwise have expired over the next several years. As a result, we incurred income tax expense of \$3.1 million, which relates to U.S. Federal and New York State alternative minimum tax and includes \$0.2 million of interest and penalties.

**Accounting for Fair Value of Financial Assets**

We consider our marketable securities, which consist primarily of U.S. government, corporate, and asset-backed securities, to be available-for-sale, as defined by SFAS 115, *Accounting for Certain Investments in Debt and Equity Securities*. These assets are carried at fair value and the unrealized gains and losses are included in other accumulated comprehensive income (loss) as a separate component of stockholders' equity. If the decline in the value of a marketable security in our investment portfolio is deemed to be other-than-temporary, we write down the security to its current fair value and recognize a loss that is charged against income.

On a quarterly basis, we review our portfolio of marketable securities, using both quantitative and qualitative factors, to determine if declines in fair value below cost are other-than-temporary. Such factors include the length of time and the extent to which market value has been less than cost, financial condition and near-term prospects of the issuer, recommendations of investment advisors, and forecasts of economic, market, or industry trends. This review process also includes an evaluation of our ability and intent to hold individual securities until they mature or their full cost can be recovered. This review is subjective and requires a high degree of judgment.

As a result of our quarterly reviews of our marketable securities portfolio, during the three and nine months ended September 30, 2008, we recorded charges for other-than-temporary impairment of our marketable securities totaling \$1.7 million and \$2.3 million, respectively. However, the current economic environment, the deterioration in the credit quality of some of the issuers of securities that we hold, and the recent volatility of securities markets increase the risk that there may be further declines in the market value of marketable securities in our investment

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portfolio and that such declines may result in additional charges against income in future periods for other-than-temporary impairments, and such amounts may be material.

In September 2006, the Financial Accounting Standards Board (FASB) 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. In addition, in October 2008, the FASB issued FASB Staff Position (FSP) 157-3, *Determining the Fair Value of a Financial Asset When the Market for That Asset Is Not Active*, which clarifies the application of SFAS 157 in a market that is not active. FSP 157-3 also reaffirms the notion of fair value as an exit price as of the measurement date. FSP 157-3 was effective upon issuance for financial statements that have not yet been issued. We adopted FSP 157-3 for the quarter ended September 30, 2008.

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 \$376.5 million as of September 30, 2008. At September 30, 2008, less than 1% of our marketable securities represented Level 3 assets.

Changes in Level 3 marketable securities during the nine months ended September 30, 2008 were as follows:

<i>(In millions)</i>	<b>Level 3 marketable securities</b>
Balance January 1, 2008	\$ 7.9
Settlements	(8.0)
Realized gain	0.9
Impairments	(0.5)
Balance September 30, 2008	\$ 0.3

During the nine months ended September 30, 2008, there were no transfers of marketable securities between Level 2 and Level 3 classifications. We had no Level 1 marketable securities during the first nine months of 2008.

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 and we independently test a



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sample of the valuations received using an alternative third-party vendor. For valuations that we determine 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, purchases of our equity securities by our collaborators, including sanofi-aventis, revenue earned under our past and present research and development and contract manufacturing agreements, including our agreements with sanofi-aventis and Bayer HealthCare, technology licensing agreements, ARCALYST<sup>®</sup> (rilonacept) product revenue, and investment income.

#### ***Nine months ended September 30, 2008 and 2007***

At September 30, 2008, we had \$692.9 million in cash, cash equivalents, restricted cash, and marketable securities compared with \$846.3 million at December 31, 2007. In February and June 2008, we received \$20.0 million annual, non-refundable payments in connection with our non-exclusive license agreements with AstraZeneca and Astellas, respectively.

#### ***Cash Used in Operations:***

Net cash used in operations was \$53.2 million in the first nine months of 2008 compared to \$23.4 million in the first nine months of 2007. Our net losses of \$51.2 million in the first nine months of 2008 and \$92.5 million in the first nine months of 2007 included \$24.7 million and \$20.5 million, respectively, of Non-cash Compensation Expense.

At September 30, 2008, accounts receivable increased by \$23.9 million, compared to end-of-year 2007, primarily due to a higher receivable balance related to our antibody collaboration with sanofi-aventis. Also, our deferred revenue balances at September 30, 2008 decreased by \$10.1 million, compared to end-of-year 2007, primarily due to the amortization of previously received deferred payments under our collaborations with sanofi-aventis and Bayer HealthCare. This decrease was partly offset by (i) the receipt of the \$20.0 million payments from AstraZeneca and Astella, as described above, which were deferred and are being recognized ratably over the ensuing year, and (ii) deferral of \$3.8 million of ARCALYST net product sales at September 30, 2008, as described above.

At September 30, 2007, our deferred revenue balances increased by \$46.8 million, compared to end-of-year 2006, due, in part, to the initial \$20.0 million up-front payments received from each of AstraZeneca and Astellas. These up-front payments have been recognized as revenue ratably over approximately the ensuing year of each non-exclusive license agreement. In addition, for the first nine months of 2007, the \$20.0 million development milestone payment received from Bayer HealthCare in August 2007 and reimbursements from Bayer HealthCare of our 2007 VEGF Trap-Eye development expenses, totaling \$12.9 million, were fully deferred and included in deferred revenue for financial statement purposes, as described above.

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*Cash Used in Investing Activities:*

Net cash used in investing activities was \$53.9 million in the first nine months of 2008, compared to \$122.2 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 nine months of 2008, purchases of marketable securities exceeded sales or maturities by \$34.7 million, whereas in the first nine months of 2007, purchases of marketable securities exceeded sales or maturities by \$114.5 million. In addition, cash used for capital expenditures totaled \$19.1 million in the first nine months of 2008, partly 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.

*Cash (Used in) Provided by Financing Activities:*

Cash used in financing activities was \$77.1 million in the first nine months of 2008 compared to cash provided by financing activities of \$5.2 million in the same period of 2007. In the first nine months of 2008, the Company repurchased \$82.5 million in principal amount of our convertible senior subordinated notes for \$83.3 million.

***Velocigene® Agreement with the sanofi-aventis Group***

As described above, in August 2008, we entered into an agreement with sanofi-aventis to use our proprietary *VelociGene* technology platform to supply sanofi-aventis with genetically modified mammalian models of gene function and disease. The agreement provides provisions for minimum annual order quantities for the term of the agreement, which extends through December 2012, for which we expect to receive payments totaling a minimum of \$21.5 million.

***Capital Expenditures:***

Our additions to property, plant, and equipment totaled \$22.5 million and \$7.9 million for the first nine months of 2008 and 2007, respectively. During the remainder of 2008, we expect to incur approximately \$20 to \$30 million in capital expenditures primarily in connection with expanding our manufacturing capacity at our Rensselaer facilities and tenant improvements and related costs in connection with our new Tarrytown operating lease. We expect that approximately \$15 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. During the first nine months of 2008, we repurchased \$82.5 million in principal amount of our notes for \$83.3 million. The remaining \$117.5 million of outstanding convertible notes were repaid in full upon their maturity in October 2008.

**Table of Contents*****License Agreement with Collectis:***

As described above, in July 2008, we and Collectis entered into an Amended and Restated Non-Exclusive License Agreement. Pursuant to the amended license agreement, in July 2008, we made a non-refundable \$12.5 million payment to Collectis and agreed to pay Collectis a low single-digit royalty based on revenue received by us from any future licenses or sales of our *VelociGene*<sup>®</sup> or *VelocImmune*<sup>®</sup> products and services. No royalties are payable with respect to our *VelocImmune* license agreements with AstraZeneca and Astellas or our November 2007 collaboration with sanofi-aventis. Moreover, no royalties are payable on any revenue from commercial sales of antibodies from our *VelocImmune* technology.

In July 2008, we and Collectis also entered into a Subscription Agreement pursuant to which we would purchase 368,301 ordinary shares of Collectis at a price of EUR 8.63 per share (which is equivalent to \$12.15 at the September 30<sup>th</sup> EUR exchange rate). The purchase was contingent upon approval by the board of directors of Collectis and by the shareholders of Collectis. Such approval was obtained on October 30, 2008, and our purchase of the Collectis shares will be completed in early November 2008.

***Amendment to Operating Lease Tarrytown, New York Facilities:***

We currently lease approximately 248,000 square feet of laboratory and office facilities in Tarrytown, New York. In December 2006, we entered into a new operating lease agreement (as amended in October 2007) to lease approximately 257,000 square feet of laboratory and office space at our current Tarrytown location, which includes approximately 27,000 square feet that would be retained from our current space and approximately 230,000 square feet in new facilities that are currently under construction and expected to be completed in mid-2009. In September 2008, we amended the operating lease agreement to increase the amount of retained space we will lease from approximately 27,000 square feet to approximately 118,000 square feet, for an amended total under the new lease of approximately 348,000 square feet. The term of the lease commenced effective June 2008 and will expire in June 2024. Other terms and conditions, as previously described in our Annual Report on Form 10-K for the year ended December 31, 2007, remain unchanged.

***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 repayment of our remaining outstanding convertible debt in October 2008, as described above, and exclusive of product revenues and costs in connection with ARCALYST<sup>®</sup> (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<sup>®</sup> (rilonacept) for the treatment of CAPS will not materially enhance or otherwise materially impact our cash flows.

In connection with the amendment to our new operating lease agreement on our Tarrytown facilities, as described above, our funding requirements for operating leases, previously disclosed in our Annual Report on Form 10-K for the year ended December 31, 2007, will increase for (1) the two-year period beginning January 1, 2009, from \$24.6 million to \$27.5 million, (2) for the two-year period beginning January 1, 2011, from \$29.7 million to \$35.2 million, and (3) for fiscal years beginning January 1, 2013 and thereafter, from \$193.6 million to \$230.3 million.

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. Currently we are required to remit royalties on product sales of ARCALYST for the treatment of CAPS. In the future, if we are able to successfully develop, market, and sell ARCALYST for other indications or 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 continued commercialization of ARCALYST and the cost of selected 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 September 30, 2008, we had no established banking arrangements through which we could obtain short-term financing or a line of credit. In the

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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.

In March 2008, the FASB issued SFAS 161, *Disclosures about Derivative Instruments and Hedging Activities* an Amendment of FASB Statement 133. SFAS 161 enhances required disclosures regarding derivatives and hedging activities, including enhanced disclosures regarding how (a) an entity uses derivative instruments, (b) derivative instruments and related hedged items are accounted for under SFAS 133, *Accounting for Derivative Instruments and Hedging Activities*, and (c) derivative instruments and related hedged items affect an entity's financial position, financial performance, and cash flows. SFAS 161 is effective for fiscal years and interim periods beginning after November 15, 2008. We are required to adopt SFAS 161 for the fiscal year beginning January 1, 2009. Our management does not anticipate that the adoption of SFAS 161 will have a material impact on our financial statements.

In April 2008, the FASB issued FASB Staff Position (FSP) FAS 142-3, *Determination of the Useful Life of Intangible Assets*. This FSP amends the factors that should be considered in developing renewal or extension assumptions used to determine the useful life of a recognized intangible asset under SFAS 142, *Goodwill and Other Intangible Assets*. The intent of this FSP is to improve the consistency between the useful life of a recognized intangible asset under SFAS 142 and the period of expected cash flows used to measure the fair value of the asset under SFAS 141R, and other generally accepted accounting principles (GAAP). This FSP is effective for fiscal years beginning after December 15, 2008. Early adoption is prohibited. We are required to adopt FSP FAS 142-3 for the fiscal year beginning January 1, 2009. Our management does not anticipate that the adoption of this FSP will have a material impact on our financial statements.

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In May 2008, the FASB issued SFAS 162, *The Hierarchy of Generally Accepted Accounting Principles*. SFAS 162 identifies the sources of accounting principles and the framework for selecting the principles used in the preparation of financial statements of nongovernmental entities that are presented in conformity with GAAP in the United States. Any effect of applying the provisions of SFAS 162 shall be reported as a change in accounting principle in accordance with SFAS 154, *Accounting Changes and Error Corrections*. SFAS 162 is effective November 15, 2008. Our management does not anticipate that the adoption of SFAS 162 will have a material impact on our financial statements.

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

#### *Interest Rate Risk:*

Our earnings and cash flows are subject to fluctuations due to changes in interest rates primarily from our investment of available cash balances in U.S. government securities, corporate, and asset-backed 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 \$1.7 million and \$2.2 million decrease in the fair value of our investment portfolio at September 30, 2008 and 2007, respectively. The decrease in the potential impact of an interest rate change at September 30, 2008 compared to September 30, 2007 is due primarily to decreases in our investment portfolio's duration at the end of September 30, 2008 versus September 30, 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 from two issuers which we considered to be other than temporarily impaired in value. In the first nine months of 2008, an additional \$0.5 million impairment charge was recognized related to one of these securities and a \$1.7 million charge was recognized related to another marketable security 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 September 30, 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**

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

**Item 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 September 30, 2008, we had a cumulative loss of \$844.4 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 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.

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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.

***The value of our marketable securities is influenced by varying economic and market conditions, and a decrease in their value may result in recognition of a loss charged against income.***

We have invested available cash balances primarily in U.S. government, corporate, and asset-backed securities, which we consider to be available-for-sale, as defined by SFAS 115, *Accounting for Certain Investments in Debt and Equity Securities*. Marketable securities totaled \$376.5 million, and represented 46% of our total assets at September 30, 2008. These assets are carried at fair value and the unrealized gains and losses are included in other accumulated comprehensive income (loss) as a separate component of stockholders' equity. If the decline in the value of a marketable security in our investment portfolio is deemed to be other-than-temporary, we write down the security to its current fair value and recognize a loss that is charged against income.

On a quarterly basis, we review our portfolio of marketable securities, using both quantitative and qualitative factors, to determine if declines in fair value below cost are other-than-temporary. Such factors include the length of time and the extent to which market value has been less than cost, financial condition and near-term prospects of the issuer, recommendations of investment advisors, and forecasts of economic, market, or industry trends. This review process also includes an evaluation of our ability and intent to hold individual securities until they mature or their full cost can be recovered. This review is subjective and requires a high degree of judgment.

As a result of our quarterly reviews of our marketable securities portfolio, during the nine months ended September 30, 2008, we recorded charges for other-than-temporary impairment of our marketable securities totaling \$2.3 million. However, the current economic environment, the deterioration in the credit quality of some of the issuers of securities that we hold, and the recent volatility of securities markets increase the risk that there may be further declines in the market value of marketable securities in our investment portfolio and that such declines may result in additional charges against income in future periods for other-than-temporary impairments, and such amounts may be material.

### **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



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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, ARCALYST® (rilonacept), and REGN88 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, ARCALYST in a variety of systemic inflammatory disorders, and REGN88 in a phase 1 rheumatoid arthritis trial. 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

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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.

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® (rilonacept) 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

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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 CAPS after treatment with ARCALYST. 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.***

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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.***

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*<sup>®</sup> 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

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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.

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.

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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. 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. 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. 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

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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.

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, Massachusetts, 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

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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 opt-out of their development, we would be required to fund and oversee on our own the clinical



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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 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

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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 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

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with regulatory requirements. If we are unable to supply sufficient material on acceptable terms, or if we should encounter delays or difficulties in our relationships with our corporate collaborators or contract manufacturers, our business, financial condition, and results of operations may be materially harmed.

We 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® (riloncept) 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.

***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

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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 in the United States and have only a small staff with commercial capabilities. We have no sales, marketing, commercial, or distribution capabilities outside the United States. 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 our products. 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. Although the incidence rate of CAPS in Europe has not been reported, it is known to be a rare set of diseases. 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® (bevacizumab) (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, ranibizumab (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 has initiated a Phase 3 trial comparing 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 impair our ability to successfully 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. For example, we have announced plans to initiate a Phase 3 program studying the use of ARCALYST for the treatment of gout flares in patients initiating urate-lowering drug therapy. Patients suffering from this disease are currently treated with inexpensive therapies, including non-steroidal inflammatory drugs. These existing treatment options are likely to be considerably less expensive and may be preferable to a biologic medication for some patients. Our future revenues and profitability will be adversely affected if United States and foreign governmental, private third-party insurers and payers, and other third-party payers,

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

We 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.

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**Risk Related to Employees**

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

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

**Risks Related to Our Common Stock**

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

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

- progress, delays, or adverse results in clinical trials;
- announcement of technological innovations or product candidates by us or competitors;
- fluctuations in our operating results;
- 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 September 30, 2008, our five largest shareholders plus Leonard S. Schleifer, M.D.



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Ph.D., our Chief Executive Officer, beneficially owned 54.7% of our outstanding shares of Common Stock, assuming, in the case of our Chief Executive Officer, the conversion of his Class A Stock into Common Stock and the exercise of all options held by him which are exercisable within 60 days of September 30, 2008. As of September 30, 2008, sanofi-aventis beneficially owned 14,799,552 shares of Common Stock, representing approximately 19.1% 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 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 September 30, 2008, holders of Class A Stock held 22.6% 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 us 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 September 30, 2008:

our current executive officers and directors beneficially owned 12.3% of our outstanding shares of Common Stock, assuming conversion of their Class A Stock into Common Stock and the exercise of all options held by such persons which are exercisable within 60 days of September 30, 2008, and 27.3% 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 September 30, 2008; and

our five largest shareholders plus Leonard S. Schleifer, M.D., Ph.D., our Chief Executive Officer, beneficially owned 54.7% of our outstanding shares of Common Stock, assuming, in the case of our Chief Executive Officer, the conversion of his Class A Stock into Common Stock and the exercise of all options held by him which are exercisable within 60 days of September 30, 2008. In addition, these six shareholders held 58.6% of the combined voting power of our outstanding shares of Common Stock and Class A Stock, assuming the exercise of all options held by our Chief Executive Officer which are exercisable within 60 days of September 30, 2008.

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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.

***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

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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 Amended and Restated 2000 Long-Term Incentive Plan may become fully vested in connection with a change in control of our company, as defined in the plan.

**Item 2. Unregistered Sales of Equity Securities and Use of Proceeds**

Issuer Purchases of 5.5% Convertible Senior Subordinated Notes due October 17, 2008:

<b>Period</b>	<b>Total principal amount purchased (1)</b>	<b>Average price paid per \$1,000 principal amount</b>	<b>Total principal amount purchased as part of publicly announced plans or programs</b>	<b>Maximum number of principal amount that may yet be purchased under the plans or programs</b>
July 1, 2008 to July 31, 2008	\$1,150,000	\$ 1,005.00	\$ 1,150,000	\$ 117,503,000

August 1, 2008 to August 31, 2008

September 1, 2008 to September 30, 2008

(1) In July 2008, through privately negotiated transactions, we repurchased \$1,150,000 aggregate principal amount of our 5.5% Convertible Senior Subordinated Notes due October 17, 2008 (the Notes). The redemption price was \$1,005 per \$1,000 principal amount

outstanding,  
plus \$13.29 of  
accrued but  
unpaid interest  
per \$1,000  
principal  
amount  
outstanding. As  
previously  
disclosed in our  
Current Report  
on Form 8-K  
filed with the  
Securities and  
Exchange  
Commission on  
June 4, 2008,  
our board of  
directors  
previously  
authorized the  
repurchase of up  
to the then  
remaining  
\$150.0 million  
in outstanding  
Notes. The  
remaining  
\$117.5 million  
of outstanding  
Notes disclosed  
in the table  
above were  
repaid in full  
upon their  
maturity in  
October 2008.

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**Item 6. Exhibits**

(a) Exhibits

**Exhibit**

**Number**

**Description**

10.1*	(a)	Amended and Restated Non-Exclusive License Agreement, dated as of July 1, 2008 by and between Cellectis, S.A. and Regeneron Pharmaceuticals, Inc.
10.2	(a)	Subscription Agreement, dated as of July 1, 2008 by and between Cellectis, S.A. and Regeneron Pharmaceuticals, Inc.
10.3		Second Amendment to Lease, by and between BMR-Landmark at Eastview LLC and Regeneron Pharmaceuticals, Inc., effective as of September 30, 2008.
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.

**Description:**

- (a) Incorporated by reference from the Form 10-Q for Regeneron Pharmaceuticals, Inc., for the quarter ended June 30, 2008, filed August 1, 2008.

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

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**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: November 5, 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)