INTERMOUNTAIN COMMUNITY BANCORP
Form 10-Q
May 12, 2008

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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549
FORM 10-Q

(Mark One)

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

FOR THE QUARTERLY PERIOD ENDED March 31, 2008

OR

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

FOR THE TRANSITION PERIOD FROM TO

Commission File Number 000-50667

INTERMOUNTAIN COMMUNITY BANCORP

(Exact name of registrant as specified in its charter)

Idaho	**82-0499463**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

414 Church Street, Sandpoint, Idaho 83864

(Address of principal executive offices) (Zip Code)

(208) 263-0505

(Registrant s telephone number, including area code)

231 North Third Avenue, Sandpoint, Idaho 83864

(Former name, former address and former fiscal year, if changed since last report)

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

Indicate by check mark 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 o Accelerated filer þ Non-accelerated filer o Smaller reporting company o
(Do not check if a smaller reporting company)

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

Indicate the number of shares outstanding of each of the issuer s classes of common stock as of the latest practicable date:

Class	**Outstanding as of May 5, 2008**
Common Stock (no par value)	8,283,613

Intermountain Community Bancorp
FORM 10-Q
For the Quarter Ended March 31, 2008

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PART I Financial Information
Item 1 Financial Statements
Intermountain Community Bancorp
Consolidated Balance Sheets
(Unaudited)

	March 31, 2008	December 31, 2007
	(Dollars in thousands)	
ASSETS:		
Cash and cash equivalents:		
Interest bearing	$ 1,134	$ 149
Non-interest bearing and vault	25,392	26,851
Restricted cash	406	4,527
Federal funds sold	3,125	6,565
Available-for-sale securities, at fair value	143,518	158,791
Held-to-maturity securities, at amortized cost	11,293	11,324
Federal Home Loan Bank of Seattle (FHLB) stock, at cost	1,779	1,779
Loans held for sale	3,143	4,201
Loans receivable, net	748,349	756,549
Accrued interest receivable	6,899	8,207
Office properties and equipment, net	44,701	42,090
Bank-owned life insurance	7,788	7,713
Goodwill	11,662	11,662
Other intangible assets	686	723
Prepaid expenses and other assets, net	7,826	7,528
Total assets	$ 1,017,701	$ 1,048,659
LIABILITIES:		
Deposits	$ 727,148	$ 757,838
Securities sold subject to repurchase agreements	105,006	124,127
Advances from Federal Home Loan Bank of Seattle	29,000	29,000
Cashier checks issued and payable	1,058	1,509
Accrued interest payable	2,155	3,027
Other borrowings	55,402	36,998
Accrued expenses and other liabilities	5,650	6,041
Total liabilities	925,419	958,540
Commitments and contingent liabilities		
STOCKHOLDERS EQUITY:		
Common stock, no par value; 29,040,000 shares authorized; 8,371,979 and 8,313,005 shares issued and 8,283,176 and 8,248,710 shares outstanding	76,746	76,746
Accumulated other comprehensive income	2,070	1,327
Retained earnings	13,466	12,046

Total stockholders equity	92,282	90,119
Total liabilities and stockholders equity	$ 1,017,701	$ 1,048,659

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

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Intermountain Community Bancorp
Consolidated Statements of Income
(Unaudited)

	Three Months Ended March 31, 2008	Three Months Ended March 31, 2007
	(Dollars in thousands, except per share data)	
Interest income:		
Loans	$ 15,017	$ 15,061
Investments	2,184	1,995
Total interest income	17,201	17,056
Interest expense:		
Deposits	4,029	4,434
Other borrowings	1,846	1,774
Total interest expense	5,875	6,208
Net interest income	11,326	10,848
(Provision for) recovery of losses on loans	(258)	(834)
Net interest income after provision for and recovery of losses on loans	11,068	10,014
Other income:		
Fees and service charges	2,004	1,787
Mortgage banking operations	406	730
Bank-owned life insurance	74	77
Other	294	447
Total other income	2,778	3,041
Operating expenses	11,259	9,677
Income before income taxes	2,587	3,378
Income tax provision	(933)	(1,285)

Net income	$	1,654	$	2,093
Earnings per share basic	$	0.20	$	0.26
Earnings per share diluted	$	0.19	$	0.24
Weighted average shares outstanding basic		8,271,104		8,161,310
Weighted average shares outstanding diluted		8,564,618		8,615,307

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

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Intermountain Community Bancorp
Consolidated Statements of Cash Flows
(Unaudited)

	Three Months Ended March 31,	
	2008	2007
	(Dollars in thousands)	
Cash flows from operating activities:		
Net income	$ 1,654	$ 2,093
Adjustments to reconcile net income to net cash provided by operating activities:		
Depreciation	759	576
Stock-based compensation expense	166	76
Net accretion of premiums on securities	(107)	(155)
Excess tax benefit related to stock-based compensation		(188)
Provisions for and (recoveries of) losses on loans	258	834
Accretion of core deposit intangibles	37	40
Gain on sale of loans, investments, property and equipment	(152)	(141)
Gain on sale of other real estate owned	(21)	
Accretion of deferred gain on sale of branch property	(4)	(4)
Net accretion of loan and deposit discounts and premiums	(6)	(11)
Increase in cash surrender value of bank-owned life insurance	(75)	(77)
Change in:		
Loans held for sale	1,058	4,197
Accrued interest receivable	1,308	821
Prepaid expenses and other assets	(1,174)	(1,426)
Accrued interest payable	(872)	300
Accrued expenses and other liabilities	(1,227)	(1,467)
Net cash provided by operating activities	1,602	5,468
Cash flows from investing activities:		
Purchases of available-for-sale securities		(23,929)
Proceeds from calls or maturities of available-for-sale securities	13,590	41,224
Principal payments on mortgage-backed securities	3,033	1,759
Proceeds from calls or maturities of held-to-maturity securities	18	42
Origination of loans, net of principal payments	2,406	(22,292)
Proceeds from sale of loans	6,198	935
Proceeds from sale of other real estate owned	62	
Purchase of office properties and equipment	(3,369)	(4,425)
Proceeds from sale of office properties and equipment		2,244
Net change in federal funds sold	3,440	(18,865)
Improvements and other changes in other real estate owned		280
Net decrease in restricted cash	4,121	356
Net cash (used in) provided by investing activities	29,499	(22,671)

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Intermountain Community Bancorp
Consolidated Statements of Cash Flows (continued)
(Unaudited)

	Three Months Ended March 31,	
	2008	2007
	(Dollars in thousands)	
Cash flows from financing activities:		
Net change in demand, money market and savings deposits	$ (22,079)	$ 35,010
Net change in certificates of deposit	(8,613)	(13,411)
Net change in repurchase agreements	(19,121)	(14,018)
Principal reduction of note payable	(13)	(9)
Excess tax benefit related to stock-based compensation		188
Acquisition of treasury stock	(190)	
Proceeds from exercise of stock options	24	152
Proceeds from other borrowings	18,417	2,446
Net cash (used in) provided by financing activities	(31,575)	10,358
Net change in cash and cash equivalents	(474)	(6,845)
Cash and cash equivalents, beginning of period	27,000	24,377
Cash and cash equivalents, end of period	$ 26,526	$ 17,532
Supplemental disclosures of cash flow information:		
Cash paid during the period for:		
Interest	$ 6,080	$ 7,099
Income taxes	375	475
Noncash investing and financing activities:		
Restricted stock issued	521	684
Deferred gain on sale/leaseback		312
Loans converted to other real estate owned	502	

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

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Intermountain Community Bancorp
Consolidated Statements of Comprehensive Income
(Unaudited)

	Three Months Ended March 31,	
	2008	**2007**
	(Dollars in thousands)	
Net income	$ 1,654	$ 2,093
Other comprehensive income:		
Change in unrealized gains on investments, net of reclassification adjustments	1,231	529
Less deferred income tax benefit	(488)	(209)
Net other comprehensive income	743	320
Comprehensive income	$ 2,397	$ 2,413

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

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Intermountain Community Bancorp
Notes to Consolidated Financial Statements

1. **Basis of Presentation**:

The foregoing unaudited interim consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States of America for interim financial information and with the instructions to Form 10-Q and Article 10 of Regulation S-X as promulgated by the Securities and Exchange Commission. Accordingly, these financial statements do not include all of the disclosures required by accounting principles generally accepted in the United States of America for complete financial statements. These unaudited interim consolidated financial statements should be read in conjunction with the audited consolidated financial statements for the year ended December 31, 2007. In the opinion of management, the unaudited interim consolidated financial statements furnished herein include adjustments, all of which are of a normal recurring nature, necessary for a fair statement of the results for the interim periods presented.

The preparation of financial statements in accordance with accounting principles generally accepted in the United States of America requires the use of estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities known to exist as of the date the financial statements are published, and the reported amounts of revenues and expenses during the reporting period. Uncertainties with respect to such estimates and assumptions are inherent in the preparation of Intermountain Community Bancorp s (Intermountain or the Company) consolidated financial statements; accordingly, it is possible that the actual results could differ from these estimates and assumptions, which could have a material effect on the reported amounts of Intermountain s consolidated financial position and results of operations.

2. **Advances from the Federal Home Loan Bank of Seattle**:

During June of 2003 the Bank obtained an advance from the Federal Home Loan Bank of Seattle (FHLB Seattle) in the amount of $5,000,000. The note is due in May 2008 with interest only payable monthly at 2.71%. During September 2007, the Bank obtained two advances from the FHLB Seattle in the amounts of $10.0 million and $14.0 million with interest only payable at 4.96% and 4.90% and maturities in September 2010 and September 2009, respectively. The Bank also had a $4.0 million cash management advance from the FHLB Seattle with a maturity of April 1, 2008 and an interest rate of 3.35%. This advance is classified as federal funds purchased with other borrowings on the balance sheet.

Advances from FHLB Seattle are collateralized by certain qualifying loans with a carrying value of approximately $29.0 million at March 31, 2008. The Bank s credit line with FHLB Seattle is limited to a percentage of its total regulatory assets subject to collateralization requirements. At March 31, 2008, Intermountain had the ability to borrow an additional $52.9 million from FHLB Seattle. Intermountain would be able to borrow amounts in excess of this total from the FHLB Seattle with the placement of additional available collateral.

3. **Other Borrowings**:

The components of other borrowings are as follows (in thousands):

	March 31, 2008	December 31, 2007
Term note payable (1)	$ 8,279	$ 8,279
Term note payable (2)	8,248	8,248

Term note payable (3)	970	982
Term note payable (4)	21,795	19,489
Federal funds purchased (5)	16,110	
Total other borrowings	$ 55,402	$ 36,998

(1) In January 2003, the Company issued $8.0 million of Trust Preferred securities through its subsidiary, Intermountain Statutory Trust I. The debt associated with these securities bore a fixed interest rate for a period of five years from issue date and now bears interest on a variable basis tied to the 90-day LIBOR (London Inter-Bank Offering Rate) index plus 3.25%, with interest only paid quarterly. The rate on this

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borrowing was 5.86% at March 31, 2008. The debt is callable by the Company in March 2008 and matures in March 2033. See Note A.

(2) In March 2004, the Company issued $8.0 million of Trust Preferred securities through its subsidiary, Intermountain Statutory Trust II. The debt associated with these securities bears interest on a variable basis tied to the 90-day LIBOR index plus 2.8%, with interest only paid quarterly. The rate on this borrowing was 7.10% at March 31, 2008. The debt is callable by the Company after five years and matures in April 2034. See Note A.

(3) In January 2006, the Company purchased land to build its new headquarters, the Sandpoint

Center in Sandpoint, Idaho. It entered into a Note Payable with the sellers of the property in the amount of $1.13 million, with a fixed rate of 6.65%. The note matures in February 2026.

(4) In December 2007, the Company renewed a borrowing agreement with Pacific Coast Bankers Bank in the amount of $25.0 million. The borrowing agreement is a revolving line of credit with a variable rate of interest tied to LIBOR with a maturity date of January 18, 2009. The collateral for the credit line is all of Panhandle State Bank s stock and the Sandpoint Center, which is currently under construction. Under the restrictive covenants of the borrowing agreement, Intermountain cannot incur additional debt

outside of its normal course of business over $5.0 million without Pacific Coast Banker s Bank s consent, and Intermountain is obligated to provide information regarding the loan portfolio on a regular basis. At March 31, 2008, the balance outstanding was $21,795,000 at a rate of 4.57%.

(5) The Company had overnight borrowings in the amount of $16,110,000 with a weighted average interest rate of 2.90% and a maturity of April 1, 2008. Included in overnight borrowings was a $4.0 million cash management advance from the FHLB Seattle.

A) Intermountain s obligations under the above debentures issued by its subsidiaries constitute a full and unconditional guarantee by Intermountain of the Statutory Trusts obligations under the Trust Preferred Securities. In accordance with Financial Interpretation No. 46 (Revised), Consolidation of Variable Interest Entities (FIN No. 46R), the trusts are not consolidated and the debentures and related amounts are treated as debt of Intermountain.

4. <u>Earnings Per Share</u>:

The following table presents the basic and diluted earnings per share computations:

Three Months Ended March 31,
(Dollars in thousands, except per share amounts)

	2008			2007		
	Net Income	**Weighted Avg. Shares**	**Per Share Amount**	**Net Income**	**Weighted Avg. Shares**	**Per Share Amount**
Basic computations	$ 1,654	8,271,104	$ 0.20	$ 2,093	8,161,310	$ 0.26
Effect of dilutive securities: Common stock options and stock grants		293,514	(0.01)		453,997	(0.02)
Diluted computations	$ 1,654	8,564,618	$ 0.19	$ 2,093	8,615,307	$ 0.24

5. <u>Operating Expenses</u>:

The following table details Intermountain s components of total operating expenses:

	Three Months Ended March 31,	
	2008	**2007**
	(Dollars in thousands)	
Salaries and employee benefits	$ 6,946	$ 6,120
Occupancy expense	1,652	1,392

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	Three Months Ended March 31, 2008	2007
	(Dollars in thousands)	
Advertising	266	219
Fees and service charges	434	278
Printing, postage and supplies	349	346
Legal and accounting	448	273
Other expense	1,164	1,049
Total operating expenses	$ 11,259	$ 9,677

6. Stock-Based Compensation Plans:

The Company utilizes its stock to compensate employees and Directors under the 1999 Director Stock Option Plan, the 1999 Employee Plan and the 1988 Employee Plan (together the Stock Option Plans). Options to purchase Intermountain common stock have been granted to employees and directors under the Stock Option Plans at prices equal to the fair market value of the underlying stock on the dates the options were granted. The options vest 20% per year, over a five-year period, and expire in 10 years. At March 31, 2008, there were 212,687 shares available for grant. The Company did not grant options to purchase Intermountain common stock during either the three months ended March 31, 2008 or 2007.

For the periods ended March 31, 2008 and 2007, stock option expense totaled $34,000 and $32,000, respectively. The Company has approximately $101,000 remaining to expense related to the non-vested stock options outstanding at March 31, 2008. This expense will be recorded over a weighted average period of 9.0 months. The expense for the stock options was calculated using the Black-Scholes valuation model per Statement 123 (R). Assumptions used in the Black-Scholes option-pricing model for options issued in years prior to 2005 are as follows:

Dividend yield	0.0%
Expected volatility	17.0% - 46.6%
Risk free interest rates	4.0% - 7.1%
Expected option lives	5 - 10 years

In 2003, shareholders approved a change to the 1999 Employee Option Plan to provide for the granting of restricted stock awards. The Company has granted restricted stock to directors and employees beginning in 2005. The restricted stock vests 20% per year, over a five-year period. The Company granted 35,949 and 28,497 restricted shares with a grant date fair value of $521,000 and $684,000 during the three months ended March 31, 2008 and 2007, respectively. For the periods ended March 31, 2008 and 2007, restricted stock expense totaled $78,000 and $32,000, respectively. Total expense related to stock-based compensation is comprised of restricted stock expense, stock option expense and expense related to the 2006-2008 Long-Term Incentive Plan (LTIP). The LTIP expense is based on anticipated company performance over a 3 year period and had a 5-year vesting period. As anticipated company performance changes, the expense related to the LTIP can fluctuate. Total expense related to stock-based compensation recorded in the three months ended March 31, 2008 and 2007 was $166,000 and $32,000, respectively.

A summary of the changes in stock options outstanding for the three months ended March 31, 2008 is presented below:

	Three months ended March 31, 2008 (dollars in thousands, except per share amounts)		
	Number of Shares	Weighted Average Exercise Price	Weighted Average Remaining life (Years)
Beginning Options Outstanding	487,329	$ 5.48	
Options Granted			
Exercises	4,945	4.86	
Ending options outstanding	482,384	5.48	2.9
Exercisable at March 31	457,006	$ 5.22	2.70

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The total intrinsic value of options exercised during the periods ended March 31, 2008 and 2007 was $43,000 and $468,000, respectively.

A summary of the Company s nonvested restricted shares for the three months ended March 31, 2008 is presented below:

Nonvested Shares	Shares	Weighted-Average Grant-Date Fair Value
Nonvested at January 1, 2008	64,295	$ 19.53
Granted	35,949	14.50
Vested	(10,863)	20.01
Forfeited	(578)	18.67
Nonvested at March 31, 2008	88,803	$ 17.44

As of March 31, 2008, there was $1.5 million of unrecognized compensation cost related to nonvested share-based compensation arrangements granted under this plan. This cost is expected to be recognized over a weighted-average period of 3.7 years.

7. Fair Value Measurements

Effective January 1, 2008, the Company adopted SFAS No. 157 (SFAS 157), *Fair Value Measurements*. SFAS 157 defines fair value, establishes a framework for measuring fair value in generally accepted accounting principles and expands disclosures about fair value measurements. SFAS 157 applies whenever other standards require (or permit) assets or liabilities to be measured at fair value but does not expand the use of fair value in any new circumstances. In this standard, the FASB clarifies the principle that fair value should be based on the assumptions market participants would use when pricing the asset or liability. In support of this principle, SFAS 157 establishes a fair value hierarchy that prioritizes the information used to develop those assumptions. The fair value hierarchy is as follows:

Level 1 inputs Unadjusted quoted process in active markets for identical assets or liabilities that the entity has the ability to access at the measurement date.

Level 2 inputs Inputs other than quoted prices included in Level 1 that are observable for the asset or liability, either directly or indirectly. These might include quoted prices for similar assets and liabilities in active markets, and inputs other than quoted prices that are observable for the asset or liability, such as interest rates and yield curves that are observable at commonly quoted intervals.

Level 3 inputs Unobservable inputs for determining the fair values of assets or liabilities that reflect an entity s own assumptions about the assumptions that market participants would use in pricing the assets or liabilities.

Available-for-sale securities is the only balance sheet category the Company is required by generally accepted accounting principles to account for at fair value. The following table presents information about the Company s assets measured at fair value on a recurring basis as of March 31, 2008, and indicates the fair value hierarchy of the valuation techniques utilized by the Company to determine such fair value (dollars in thousands).

Fair Value Measurements

		At March 31, 2008, Using		
		Quoted Prices In Active Markets for Identical Assets	Other Observable Inputs	Significant Unobservable Inputs
Description	Fair Value Mar. 31, 2008	(Level 1)	(Level 2)	(Level 3)
Available-for-Sale Securities	$ 143,518	$	$ 143,518	$
Total Assets Measured at Fair Value	**$ 143,518**	**$**	**$ 143,518**	**$**

Available for Sale Securities. Securities classified as available for sale are reported at fair value utilizing Level 2 inputs. For these securities, the Company obtains fair value measurements from an independent pricing service. The fair value measurements consider observable data that may include dealer quotes, market spreads, cash flows, the U.S. Treasury yield curve, live trading levels, trade execution data, market consensus prepayment speeds, credit information and the bond s terms and conditions, among other things.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities Including an Amendment of FASB Statement No. 115.* This Statement permits entities to choose to measure many financial instruments and certain other items at fair value. Unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings. The objective is to improve financial reporting by providing entities with the opportunity to mitigate volatility in reported earnings caused by measuring related assets and liabilities differently without having to apply complex hedge accounting provisions. This Statement is expected to expand the use of fair value measurement, which is consistent with the FASB s long-term measurement objectives for accounting for financial instruments. SFAS No. 159 is effective for fiscal years beginning after November 15, 2007. The Company has not elected the fair value option for any financial assets or liabilities at March 31, 2008.

8. Subsequent Events:

Subsequent to the end of the first quarter, as part of its interest rate and investment management program, the Company sold $32.0 million in the available for sale investment securities and reinvested the proceeds in other available-for-sale investment securities. The transaction resulted in an after-tax gain on sale of investments of approximately $1.4 million. This will be reflected in second quarter 2008 income.

9. New Accounting Policies:

In September 2006, the FASB issued Statement No. 157, Fair Value Measurements (SFAS 157). SFAS 157 defines fair value, establishes a framework for measuring fair value and expands disclosures about fair value measurements. SFAS 157 establishes a fair value hierarchy about the assumptions used to measure fair value and clarifies assumptions about risk and the effect of a restriction on the sale or use of an asset. SFAS 157 is effective for fiscal years beginning after November 15, 2007. In February 2008, the FASB issued Staff Position (FSP) 157-2, Effective Date of FASB Statement No. 157. This FSP delays the effective date of FAS 157 for all nonfinancial assets and nonfinancial liabilities, except those that are recognized or disclosed at fair value on a recurring basis (at least annually) to fiscal years beginning after November 15, 2008, and interim periods within those fiscal years. The impact of adoption was not material.

In February 2007, the FASB issued Statement No. 159, The Fair Value Option for Financial Assets and Financial Liabilities (SFAS 159). SFAS 159 provides companies with an option to report selected financial assets and liabilities at fair value and establishes presentation and disclosure requirements designed to facilitate comparisons between companies that choose different measurement attributes for similar types of assets and liabilities. The Company did not elect the fair value option for any financial assets or financial liabilities as of January 1, 2008, the effective date of the standard.

In December 2007, the FASB issued SFAS No. 160, Noncontrolling Interest in Consolidated Financial Statements (SFAS 160). SFAS 160 re-characterizes minority interests in consolidated subsidiaries as non-controlling interests and requires the classification of minority interests as a component of equity. Under SFAS 160, a change in control will be measured at fair value, with any gain or loss recognized in earnings. The effective date for SFAS 160 is for annual periods beginning on or after December 15, 2008. Early adoption and retroactive application of SFAS 160 to fiscal years preceding the effective date are not permitted. The Company is evaluating the impact of adoption on its Consolidated Financial Statements.

In March 2008, the FASB issued SFAS No. 161, Disclosures about Derivative Instruments and Hedging Activities (SFAS 161). SFAS 161 requires specific disclosures regarding the location and amounts of derivative instruments in the Company s financial statements; how derivative instruments and related hedged items are accounted for; and how derivative instruments and related hedged items affect the Company s financial position, financial performance, and cash flows. SFAS 161 is effective for financial statements issued and for fiscal years and interim periods after November 15, 2008. Early application is permitted. Because SFAS 161 impacts the Company s disclosure and not its accounting treatment for derivative instruments and related hedged items, the Company s adoption of SFAS 161 will not impact the Consolidated Financial Statements.

In September 2006, the FASB Emerging Issues Task Force finalized Issue No. 06-4 (EITF 06-4), Accounting for Deferred Compensation and Postretirement Benefit Aspects of Endorsement Split-Dollar Life

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Insurance Arrangements. EITF 06-4 requires that a liability be recorded during the service period when a split-dollar life insurance agreement continues after participants employment or retirement. The required accrued liability will be based on either the post-employment benefit cost for the continuing life insurance or based on the future death benefit depending on the contractual terms of the underlying agreement. EITF 06-4 is effective for fiscal years beginning after December 15, 2007. Effective January 1, 2008, the Company recorded a liability in the amount of $389,000 and a reduction in equity in the amount of $235,000 to record the liability as of January 1, 2008.

On November 5, 2007, the SEC issued Staff Accounting Bulletin No. 109, Written Loan Commitments Recorded at Fair Value through Earnings (SAB 109). Previously, SAB 105, Application of Accounting Principles to Loan Commitments, stated that in measuring the fair value of a derivative loan commitment, a company should not incorporate the expected net future cash flows related to the associated servicing of the loan. SAB 109 supersedes SAB 105 and indicates that the expected net future cash flows related to the associated servicing of the loan should be included in measuring fair value for all written loan commitments that are accounted for at fair value through earnings. SAB 105 also indicated that internally-developed intangible assets should not be recorded as part of the fair value of a derivative loan commitment, and SAB 109 retains that view. SAB 109 is effective for derivative loan commitments issued or modified in fiscal quarters beginning after December 15, 2007. The Company believes the impact of this standard to be immaterial.

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

This report contains forward-looking statements. For a discussion about such statements, including the risks and uncertainties inherent therein, see Forward-Looking Statements. Management s Discussion and Analysis of Financial Condition and Results of Operations should be read in conjunction with the Consolidated Financial Statements and Notes presented elsewhere in this report and in Intermountain s Form 10-K for the year ended December 31, 2007.

General

Intermountain Community Bancorp (Intermountain or the Company) is a financial holding company registered under the Bank Holding Company Act of 1956, as amended. The Company was formed as Panhandle Bancorp in October 1997 under the laws of the State of Idaho in connection with a holding company reorganization of Panhandle State Bank (the Bank) that was approved by the shareholders on November 19, 1997 and became effective on January 27, 1998. In June 2000, Panhandle Bancorp changed its name to Intermountain Community Bancorp.

Panhandle State Bank, a wholly owned subsidiary of the Company, was first opened in 1981 to serve the local banking needs of Bonner County, Idaho. Panhandle State Bank is regulated by the Idaho Department of Finance, the State of Washington Department of Financial Institutions, the Oregon Division of Finance and Corporate Securities and by the Federal Deposit Insurance Corporation (FDIC), its primary federal regulator and the insurer of its deposits.

Since opening in 1981, the Bank has continued to grow by opening additional branch offices throughout Idaho. During 1999, the Bank opened its first branch under the name of Intermountain Community Bank, a division of Panhandle State Bank, in Payette, Idaho. Over the next several years, the Bank continued to open branches under both the Intermountain Community Bank and Panhandle State Bank names. In January 2003, the Bank acquired a branch office from Household Bank F.S.B. located in Ontario, Oregon which is now operating under the Intermountain Community Bank name. In 2004, Intermountain acquired Snake River Bancorp, Inc. (Snake River) and its subsidiary bank, Magic Valley Bank, and the Bank now operates three branches under the Magic Valley Bank name in southcentral Idaho. In 2005 and 2006, the Company opened branches in Spokane Valley and downtown Spokane, Washington, respectively, and operates these branches under the name of Intermountain Community Bank of Washington. It also opened branches in Kellogg and Fruitland, Idaho.

In 2006, Intermountain also opened a Trust & Wealth division, and purchased a small investment company, Premier Alliance, which now operates as Intermountain Community Investment Services (ICI). The acquisition and development of these services improves the Company s ability to provide a full-range of financial services to its targeted customers. In 2007, the Company relocated its Spokane Valley office to a larger facility housing retail, commercial, and mortgage banking functions and administrative staff. In the first quarter, 2008, the Bank neared completion of the Sandpoint Center, its new corporate headquarters and began relocating administrative staff into the building. It expects to complete this relocation and move the Sandpoint branch to the new center in second quarter 2008.

Based on asset size at March 31, 2008, Intermountain is the largest independent commercial bank headquartered in the state of Idaho, with consolidated assets of $1.02 billion. Intermountain competes with a number of international banking groups, out-of-state banking companies, state banking organizations, local community banks, savings banks, savings and loans, and credit unions throughout its market area.

Intermountain offers banking and financial services that fit the needs of the communities it serves. Lending activities include consumer, commercial, commercial real estate, residential construction, mortgage and agricultural loans. A full range of deposit services are available including checking, savings and money market accounts as well as various types of certificates of deposit. Trust and wealth management services, investment services, and business cash management solutions round out the company s financial offerings.

Intermountain seeks to differentiate itself by attracting, retaining and motivating highly experienced employees who are local market leaders, and supporting them with advanced technology, training and compensation systems. This approach allows the Bank to provide local marketing and decision-making to respond quickly to customer opportunities and build leadership in its communities. Simultaneously, the Bank has more recently focused on standardizing and centralizing administrative and operational functions to improve efficiency and the ability of the branches to serve customers effectively.

Current Economic Challenges and Future Economic Outlook

After a long period of economic prosperity, both the nation and the Company s local markets have struggled over the past year. A slowing economy and significant downturns in real estate markets have combined with increasing inflation to create substantial challenges for the Company s customers and communities. The federal government has moved proactively to limit the damage, but in doing so has produced a dramatic drop in short-term interest rates. This combination of economic factors has impacted the Company negatively in the following ways:

- A slowdown in loan demand, as both the Bank and its borrowers respond to current conditions with increasing caution;
- Slowing deposit demand, as customers have less cash to save with rising inflation and are responding negatively to lowered deposit interest rates;
- Decreasing net interest margin, as the Company s assets, and particularly its loans, have repriced down more quickly in response to a 3.0% drop in the Federal Funds rate over the past eight months than its deposits and other liabilities;
- Higher non-performing loans and credit losses, as existing borrowers, particularly those in the real estate industry, struggle to make payments and sell assets; and
- Slowing fee income growth, particularly fees derived from mortgage banking activity

Amidst these challenges, there are some positive factors at work in the Company s markets. The economies of Idaho, eastern Washington and eastern Oregon have generally been stronger than other markets, as a result of: (1) continuing in-migration and population growth trends; (2) a strong agricultural economy; (3) a diversity of different industries, including manufacturing, natural resources, technology, health care, retail, professional services, tourism and real estate; and (4) benefits from the weak dollar due to the region s proximity to Canada and a relatively high proportion of export businesses.

As detailed in the discussion of its results below, the Company s performance has been adversely impacted by the struggling economy. The Company is responding to the current challenges by actively monitoring and managing its loan portfolio, focusing on retaining, expanding and growing its high-value customers, providing leadership and assistance in its communities, and streamlining operations. While its focus is clear, there can be no assurance that Intermountain will be successful in executing these plans.

Critical Accounting Policies

The accounting and reporting policies of Intermountain conform to Generally Accepted Accounting Principles (GAAP) and to general practices within the banking industry. The preparation of the financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates. Intermountain s management has identified the accounting policies described below as those that, due to the judgments, estimates and assumptions inherent in those policies, are critical to an understanding of Intermountain s Consolidated Financial Statements and Management s Discussion and Analysis of Financial Condition and Results of Operations.

Income Recognition. Intermountain recognizes interest income by methods that conform to general accounting practices within the banking industry. In the event management believes collection of all or a portion of contractual interest on a loan has become doubtful, which generally occurs after the loan is 90 days past due, Intermountain discontinues the accrual of interest and reverses any previously accrued interest recognized in income deemed uncollectible. Interest received on nonperforming loans is included in income only if recovery of the principal is reasonably assured. A nonperforming loan is restored to accrual status when it is brought current or when brought to 90 days or less delinquent, has performed in accordance with contractual terms for a reasonable period of time, and the collectibility of the total contractual principal and interest is no longer in doubt.

Allowance For Loan Losses. In general, determining the amount of the allowance for loan losses requires significant judgment and the use of estimates by management. This analysis is designed to determine an appropriate level and allocation of the allowance for losses among loan types and loan classifications by considering factors affecting loan losses, including: specific losses; levels and trends in impaired and nonperforming loans; historical bank and industry loan loss experience; current national and local economic conditions; volume, growth and composition of

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the portfolio; regulatory guidance; and other relevant factors. Management monitors the loan portfolio to evaluate the adequacy of the allowance. The allowance can increase or decrease based upon the results of management s analysis.

The amount of the allowance for the various loan types represents management s estimate of probable incurred losses inherent in the existing loan portfolio based upon historical bank and industry loan loss experience for each loan type. The allowance for loan losses related to impaired loans usually is based on the fair value of the collateral for certain collateral dependent loans. This evaluation requires management to make estimates of the value of the collateral and any associated holding and selling costs.

Individual loan reviews are based upon specific quantitative and qualitative criteria, including the size of the loan, loan quality classifications, value of collateral, repayment ability of borrowers, and historical experience factors. The historical experience factors utilized are based upon past loss experience, trends in losses and delinquencies, the growth of loans in particular markets and industries, and known changes in economic conditions in the particular lending markets. Allowances for homogeneous loans (such as residential mortgage loans, personal loans, etc.) are collectively evaluated based upon historical bank and industry loan loss experience, trends in losses and delinquencies, growth of loans in particular markets, and known changes in economic conditions in each particular lending market. The Allowance for Loan Losses analysis is presented to the Audit Committee for review.

Management believes the allowance for loan losses was adequate at March 31, 2008. While management uses available information to provide for loan losses, the ultimate collectibility of a substantial portion of the loan portfolio and the need for future additions to the allowance will be based on changes in economic conditions and other relevant factors. A slowdown in economic activity could adversely affect cash flows for both commercial and individual borrowers, as a result of which the Company could experience increases in nonperforming assets, delinquencies and losses on loans.

A reserve for unfunded commitments is maintained at a level that, in the opinion of management, is adequate to absorb probable losses associated with the Bank s commitment to lend funds under existing agreements such as letters or lines of credit. Management determines the adequacy of the reserve for unfunded commitments based upon reviews of individual credit facilities, current economic conditions, the risk characteristics of the various categories of commitments and other relevant factors. The reserve is based on estimates, and ultimate losses may vary from the current estimates. These estimates are evaluated on a regular basis and, as adjustments become necessary, they are recognized in earnings in the periods in which they become known through charges to other non-interest expense. Draws on unfunded commitments that are considered uncollectible at the time funds are advanced are charged to the reserve for unfunded commitments. Provisions for unfunded commitment losses, and recoveries on commitment advances previously charged-off, are added to the reserve for unfunded commitments, which is included in the accrued expenses and other liabilities section of the Consolidated Statements of Financial Condition.

Investments. Assets in the investment portfolios are initially recorded at cost, which includes any premiums and discounts. Intermountain amortizes premiums and discounts as an adjustment to interest income using the interest yield method over the life of the security. The cost of investment securities sold, and any resulting gain or loss, is based on the specific identification method.

Management determines the appropriate classification of investment securities at the time of purchase. Held-to-maturity securities are those securities that the Company has the intent and ability to hold to maturity, and are recorded at amortized cost. Available-for-sale securities are those securities that would be available to be sold in the future in response to liquidity needs, changes in market interest rates, and asset-liability management strategies, among others. Available-for-sale securities are reported at fair value, with unrealized holding gains and losses reported in stockholders equity as a separate component of other comprehensive income, net of applicable deferred income taxes.

Management evaluates investment securities for other than temporary declines in fair value on a periodic basis. If the fair value of investment securities falls below their amortized cost and the decline is deemed to be other than temporary, the securities will be written down to current market value and the write down will be deducted from earnings. There were no investment securities which management identified to be other-than-temporarily impaired for the three months ended March 31, 2008. Charges to income could occur in future periods due to a change in management s intent to hold the investments to maturity, a change in management s assessment of credit risk, or a change in regulatory or accounting requirements.

Goodwill and Other Intangible Assets**.** Goodwill arising from business combinations represents the value attributable to unidentifiable intangible elements in the business acquired. Intermountain s goodwill relates to value inherent in the banking business and the value is dependent upon Intermountain s ability to provide quality, cost effective services in a competitive market place. As such, goodwill value is supported ultimately by revenue that is

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driven by the volume of business transacted. A decline in earnings as a result of a lack of growth or the inability to deliver cost effective services over sustained periods can lead to impairment of goodwill that could adversely impact earnings in future periods. Goodwill is not amortized, but is subjected to impairment analysis periodically. No impairment was considered necessary during the three months ended March 31, 2008. However, future events could cause management to conclude that Intermountain s goodwill is impaired, which would result in the recording of an impairment loss. Any resulting impairment loss could have a material adverse impact on Intermountain s financial condition and results of operations.

Other intangible assets consisting of core-deposit intangibles with definite lives are amortized over the estimated life of the acquired depositor relationships.

Real Estate Owned. Property acquired through foreclosure of defaulted mortgage loans is carried at the lower of cost or fair value less estimated costs to sell. Development and improvement costs relating to the property are capitalized to the extent they are deemed to be recoverable.

An allowance for losses on real estate owned is designed to include amounts for estimated losses as a result of impairment in value of the real property after repossession. Intermountain reviews its real estate owned for impairment in value whenever events or circumstances indicate that the carrying value of the property may not be recoverable. In performing the review, if expected future undiscounted cash flow from the use of the property or the fair value, less selling costs, from the disposition of the property is less than its carrying value, an allowance for loss is recognized. As a result of changes in the real estate markets in which these properties are located, it is reasonably possible that the carrying values could be reduced in the near term.

Intermountain Community Bancorp

Comparison of the Three Month Periods Ended March 31, 2008 and 2007

Results of Operations

Overview. Intermountain recorded net income of $1.7 million, or $0.19 per diluted share, for the three months ended March 31, 2008, compared with net income of $2.1 million, or $0.24 per diluted share, for the three months ended March 31, 2007.

The decline in earnings reflected slowing revenue growth and increased non-interest expenses related to higher employee benefits, credit and compliance costs. Both net interest income and non-interest income have been negatively impacted by deteriorating economic conditions, as asset growth has slowed and rapidly declining market interest rates have led to compression in the Bank s net interest margin. While overall staffing levels have decreased over last year, increased costs related to credit management, regulatory compliance requirements, and higher employee benefit costs have combined to create an increase in non-interest expenses.

The annualized return on average assets was 0.64% and 0.92% for the three months ended March 31, 2008 and 2007, respectively. The annualized return on average equity was 7.3% and 10.7% for the three months ended March 31, 2008 and 2007, respectively. The decrease in both the return on average assets and the return on average equity resulted primarily from the decrease in net income, as decreases in non interest income and increases in operating expenses offset increases in net interest income.

The Company s first quarter results clearly reflect the slowing economic conditions discussed above, combined with the carryover costs of the rapid expansion that it undertook in the past five years. In adjusting to the current market environment, the Company has increased its focus on streamlining internal operations to improve both customer service and efficiency. During its recent rapid growth period, the Company had, in some ways, outpaced its internal operations. Management believes that the challenges presented by the current environment provide opportunities to improve these operations. At the same time, management continues to focus on employee morale and culture, its high-value customers and the communities in which it serves, These efforts have led to the Company s recent recognition as one of the top places to work in Idaho by the ***Idaho Business Journal***.

It appears that 2008 will be one of the most challenging years for the banking sector and Intermountain in recent memory. Management is responding by working to protect its customers, employees and shareholders in the current environment, while building effective processes and marketing for the future.

Net Interest Income. The most significant component of earnings for the Company is net interest income, which is the difference between interest income, primarily from the Company s loan and investment portfolios, and

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interest expense, primarily on deposits and other borrowings. During the three months ended March 31, 2008 and 2007, net interest income was $11.3 million and $10.8 million, respectively, an increase of 4.4%. The positive increase resulted from growth in earning assets over last year, but was somewhat offset by a lower net interest margin.

Average interest-earning assets for the three months ended March 31, 2008 and 2007 were $935.3 million and $839.3 million, respectively. The increases in the components of average interest-earning assets are primarily due to organic growth in the loan portfolio, with average loans increasing by $89.9 million. Average investments and cash increased by $6.1 million over the same period. Average net interest spread during the three months ended March 31, 2008 and 2007 was 4.84% and 5.19%, respectively. Net interest margin decreased 0.37% from 5.24%for the three months ended March 31, 2007 to 4.87% for the three months ended March 31, 2008 as the yields on earnings assets decreased at a faster pace than the cost of interest-bearing liabilities. While the prime lending rate was stable during the first half of 2007, it dropped by a total of 3.00% from August 2007 to March 2008. This rapid market rate drop caused loan yields to decrease significantly, while liability interest costs, particularly those on deposits, dropped more slowly. The Company s assets and liabilities both reprice relatively quickly, but the cost of its liabilities tends to lag its earning asset yield when market rates change substantially.

Provision for Losses on Loans. Management s policy is to establish valuation allowances for estimated losses by charging corresponding provisions against income. This evaluation is based upon management s assessment of various factors including, but not limited to, current and future economic trends, historical loan losses, delinquencies, underlying collateral values, as well as current and potential risks identified in the portfolio.

Intermountain recorded a provision for losses on loans of $258,000 for the first quarter 2008 compared to an $834,000 provision for losses on loans for the three months ended March 31, 2007. The provision reflects the analysis and assessment of the relevant factors mentioned in the preceding paragraph. The decrease is due primarily to the absence of any large credit write-downs during the quarter and a decrease in the size of the loan portfolio since December 31, 2007.

In response to current market conditions and the implementation of new federal guidance in 2007, management has expanded and refined its evaluation of the current loan portfolio and the adequacy of its loan loss allowance. The loan loss allowance to total loans ratio was 1.57% at March 31, 2008, compared to 1.52% at March 31, 2007 and 1.53% at December 31, 2007, and remains at a level that is generally higher than its national peer group. Management believes that the level of the loan loss allowance as of March 31, 2008 is adequate for the prevailing economic conditions and the balance and mix of the loan portfolio. However, a significantly deeper or prolonged worsening of the economy may have additional adverse impacts on the Company s loan portfolio, potentially causing higher future loan loss provision levels.

The following table summarizes loan loss allowance activity for the periods indicated.

	Three Months Ended March 31,	
	2008	2007
	(Dollars in thousands)	
Balance at January 1	$ 11,761	$ 9,837
Provision (recovery) for losses on loans	258	834
Amounts written off, net of recoveries	(77)	(101)
Transfers		(2)
Allowance loans, March 31	$ 11,942	$ 10,568
Allowance unfunded commitments, January 1	18	482
Transfers		2
Adjustments	(3)	
Allowance unfunded commitments, March 31	15	484

Total credit allowance	$ 11,957	$ 11,052

At March 31, 2008, Intermountain s total classified assets were $31.5 million, compared with $10.4 million at March 31, 2007 and $23.3 million at December 31, 2007. The increase in classified assets is primarily comprised of struggling residential land and construction loans, reflecting the current weakness in the housing market. Total nonperforming loans were $7.1 million at March 31, 2008, compared with $1.8 million at March 31, 2007 and $6.4 million at December 31, 2007, also reflecting weakness in housing-related loans. At March 31, 2008, Intermountain s loan delinquency rate (30 days or more) as a percentage of total loans was 1.13%, compared with 0.25% at March 31, 2007 and 0.40% at December 31, 2007. Management believes that the Company s credit quality remains stable and that it is identifying and managing potential risks proactively, but the results do reflect deterioration in asset quality levels.

Other Income. Total other income was $2.8 million and $3.0 million for the three months ended March 31, 2008 and 2007, respectively. Fees and service charge income increased by 12.1% to $2.0 million for the three months ended March 31, 2008 as debit card income, trust and investment income, merchant acceptance and cash management fees continued to increase. This increase was offset by a 44.4% drop in fees from mortgage banking operations for the quarter ended March 31, 2008 over first quarter 2007, as mortgage originations declined significantly. Contractual income from the company s secured card deposit portfolio was also lower, reflecting tighter conditions in the credit card market. Expanding the depth and breadth of the Company s non-interest revenue is a high priority for management. It is actively targeting profitable customer groups with new products, ranging from trust services to business cash management solutions.

Operating Expenses. Operating expenses were $11.3 million and $9.7 million for the three months ended March 31, 2008 and 2007, respectively. The Company s efficiency ratio increased to 79.8% for the three months ended March 31, 2008 from 69.7% in the corresponding period in 2007, impacted by both increasing expenses and a slowdown in revenue growth from the first quarter of 2007. The carry-over costs from earlier investments to develop new markets and new services, coupled with increases in staffing and technology to support heightened credit monitoring and regulatory compliance requirements were the primary contributors to the growth in operating expenses for the three months ended March 31, 2008.

Salaries and employee benefits were $6.9 million and $6.1 million for the three months ended March 31, 2008 and 2007, respectively. The rate of increase in salary expense has slowed to 7.0% over the same period last year. Additional regulatory compliance and audit staff comprised approximately 25% of the overall salary increase, with merit and promotional increases generating much of the rest. Benefits expense rose significantly as a result of a large increase in medical and dental insurance premiums at the beginning of 2008. At March 31, 2008, full-time-equivalent employees were 442, compared with 447 at March 31, 2007.

Occupancy expenses were $1.7 million and $1.4 million for the three months ended March 31, 2008 and 2007, respectively. Occupancy expense increases reflected additional building expense from new branches opened in 2006 and 2007 and additional computer hardware and software purchased to enhance security, compliance and business continuity.

Other expenses grew from $2.2 million in the first three months of 2007 to $2.7 million in the first quarter of 2008. Advertising, printing, supplies, training and travel expenses were largely flat during this period of time, However, the reinstatement of FDIC insurance premiums added $127,000 and consulting expenses added $190,000 to first quarter 2008 expenses over last year. The Company has engaged consulting assistance to improve its business processes and enhance efficiency, and expects to see the benefits of these efforts in future periods.

Management has invested heavily in human capital, buildings and technology during its rapid expansion over the past several years, as it sought to build the infrastructure needed to grow and maintain operational integrity and compliance with regulatory requirements. It is now adjusting to a changing market by working to operate more effectively and efficiently. It is completing a number of initiatives, including the implementation of branch imaging technology, automating and streamlining the loan processing function, and centralizing and standardizing certain operational functions. As these initiatives take hold this year, management believes that the Company s efficiency will improve.

Income Tax Provision. Intermountain recorded federal and state income tax provisions of $933,000 and $1.3 million for the three months ended March 31, 2008 and 2007, respectively. The decreased tax provision in 2008 from 2007 is due to the decrease in pre-tax net income and a lower effective tax rate. The effective tax rates for both the three-month periods ended March 31, 2008 and 2007 were 36.1% and 38.0%, respectively, with additional investment tax credits and other factors combining to reduce this rate.

Financial Position

Assets. At March 31, 2008, Intermountain s assets were $1.02 billion, down $31.0 million or 3.0% from $1.05 billion at December 31, 2007. The decrease in assets primarily reflected decreases in loans, short-term investments and cash.

Investments. Intermountain s investment portfolio at March 31, 2008 was $156.6 million, a decrease of $15.3 million or 8.9% from the December 31, 2007 balance of $171.9 million. The decrease was primarily due to maturity of short-term U. S. Government obligations and paydowns on mortgage-backed securities. Funds from these payments were used to help fund the decrease in deposits and paydown of repurchase agreement obligations. As of March 31, 2008, the balance of the unrealized gain, net of federal income taxes, was $2.1 million compared to an unrealized gain at December 31, 2007 of $1.3 million. Falling long-term market rates increased the market value of the securities, resulting in an increase in the unrealized gain. Subsequent to the end of the first quarter, as part of its interest rate and investment management program, the Company sold $32.0 million in investment securities, and reinvested the proceeds in other available-for-sale investment securities. The transaction resulted in an after-tax gain on sale of investments of approximately $1.4 million. This will be reflected in second quarter 2008 income.

Loans Receivable. At March 31, 2008, net loans receivable totaled $748.3 million, down $8.2 million or 1.1% from $756.5 million at December 31, 2007. The decrease reflected the slowing economy, tightening credit underwriting standards, and seasonal factors related to slower agriculture and real estate activity during the winter. During the three months ended March 31, 2008, total loan originations were $139.4 million compared with $163.9 million for the prior year s comparable period, reflecting the slowdown in activity.

The following table sets forth the composition of Intermountain s loan portfolio at the dates indicated. Loan balances exclude deferred loan origination costs and fees and allowances for loan losses.

	March 31, 2008		December 31, 2007	
	Amount	**%**	**Amount**	**%**
	(Dollars in thousands)			
Commercial	$ 229,119	30.12	$ 240,421	31.27
Commercial real estate	388,898	51.12	383,018	49.80
Residential real estate	112,653	14.81	114,010	14.83
Consumer	24,748	3.25	26,285	3.42
Municipal	5,341	0.70	5,222	0.68
Total loans receivable	760,759	100.00	768,956	100.00
Net deferred origination fees	(468)		(646)	
Allowance for losses on loans	(11,942)		(11,761)	
Loans receivable, net	$ 748,349		$ 756,549	
Weighted average yield at end of period	7.46%		8.16%	

The following table sets forth Intermountain s loan originations for the periods indicated.

	Three Months Ended March 31,		
	2008	**2007**	**% Change**
	(Dollars in thousands)		
Commercial	$ 57,899	$ 72,592	(20.2)
Commercial real estate	59,759	64,364	(7.2)
Residential real estate	18,373	21,310	(13.8)
Consumer	3,104	5,453	(43.1)
Municipal	314	200	57.0

Total loans originated	$ 139,449	$ 163,919	(14.9)

As of March 31, 2008, the Bank s loan portfolio by loan type was:

Commercial	30.12%
Commercial real estate	51.12%
Residential real estate	14.81%
Consumer	3.25%
Municipal	0.70%

These concentrations are typical for the markets served by the Bank, and management believes that they are comparable with those of the Bank s peer group (banks of similar size and operating in the same geographic areas). At March 31, 2008, approximately 66% of the total loan portfolio was secured by real estate.

The residential land and construction loan portfolio currently appears to pose the greatest overall risk of loan-type concentration. However, experienced lenders and consistently applied underwriting standards help to mitigate credit risk. Real estate values tend to fluctuate somewhat with economic conditions. Currently, valuations are static or falling in many of the Bank s markets, although the rate of decline is smaller than current national average rates of decline. Over longer periods, real estate collateral is generally considered one of the more stable forms of collateral in regards to maintaining value.

The Bank lends to contractors and developers, and is also active in custom construction lending. The Bank has established concentration limits as measured against Tier 1 capital (generally, Tier 1 capital is the Company s tangible net worth). These concentration limits include residential and commercial construction loans not to exceed 175% and, combined with development loans, not to exceed 325% of Tier 1 capital. The guidelines further specify that total commercial real estate loans are not to exceed 400% and other real estate (agricultural and land) loans are not to exceed 230% of the Bank s Tier 1 capital. Accordingly, at March 31, 2008, residential and commercial construction loans represented 112.3% and, combined with development loans, represented 279.9% of Tier 1 capital. Total commercial real estate loans represented 385.0%, and other real estate loans represented 149.9% of the Bank s Tier 1 capital, respectively. These ratios compare to December 2007 totals of 128.2%, 295.6%, 380.5% and 147.7%, respectively, generally demonstrating decreases in construction and development loans, and slight increases in other real estate and total commercial real estate loans. Those two categories increased in the first quarter due to increased loans for owner occupied consumer and commercial and non owner occupied commercial, as part of a risk diversification strategy by the Bank.

BOLI and All Other Assets. Bank-owned life insurance (BOLI) and other assets decreased to $22.5 million at March 31, 2008 from $23.4 million at December 31, 2007. The decrease was primarily due to decreases in the net deferred tax asset and accrued interest receivable, offset by an increase in other real estate owned.

Deposits. Total deposits decreased $30.7 million or 4.0% to $727.1 million at March 31, 2008 from $757.8 million at December 31, 2007, primarily due to decreases in demand accounts, money market accounts and certificates of deposits. The decrease reflected negative customer response to significantly lower rates, a tightening economy, the runoff of some high rate deposits, and normal seasonal factors. Company management continues to be very focused on core deposit growth, particularly of lower-costing demand, savings and money market deposits. Management is implementing new compensation plans, promotional strategies and products to spur local deposit growth.

The following table sets forth the composition of Intermountain s deposits at the dates indicated.

	March 31, 2008		December 31, 2007	
	Amount	%	Amount	%
	(Dollars in thousands)			
Demand	$ 151,585	20.8	$ 159,069	21.0
NOW and money market 0.0% to 5.5%	295,090	40.6	308,857	40.8
Savings and IRA 0.0% to 4.2%	86,321	11.9	87,149	11.5
Certificate of deposit accounts	194,152	26.7	202,763	26.7

Total deposits	$ 727,148	100.0	$ 757,838	100.0
Weighted average interest rate on certificates of deposit		3.91%		4.57%

Borrowings. Deposit accounts are Intermountain s primary source of funds. Intermountain also relies upon advances from the Federal Home Loan Bank of Seattle, repurchase agreements and other borrowings to supplement its funding and to meet deposit withdrawal requirements. These borrowings totaled $189.4 million and $190.1 million at March 31, 2008 and December 31, 2007, respectively. The decrease resulted from seasonal declines in municipal repurchase obligations as local governments utilized tax revenues to fund operating expenses. See Liquidity and Sources of Funds for additional information.

Interest Rate Risk

The results of operations for financial institutions may be materially and adversely affected by changes in prevailing economic conditions, including rapid changes in interest rates, declines in real estate market values and the monetary and fiscal policies of the federal government. Like all financial institutions, Intermountain s net interest income and its NPV (the net present value of financial assets, liabilities and off-balance sheet contracts), are subject to fluctuations in interest rates. Intermountain utilizes various tools to assess and manage interest rate risk, including an internal income simulation model that seeks to estimate the impact of various rate changes on the net interest income and net income of the bank. This model is validated by comparing results against various third-party estimations. Currently, the model and third-party estimates indicate that Intermountain is slightly asset-sensitive. An asset-sensitive bank generally sees improved net interest income and net income in a rising rate environment, as its assets reprice more rapidly and/or to a greater degree than its liabilities. The opposite is true in a falling interest rate environment. When market rates fall, an asset-sensitive bank tends to see declining income.

To minimize the impact of fluctuating interest rates on net interest income, Intermountain promotes a loan pricing policy of utilizing variable interest rate structures that associates loan rates to Intermountain s internal cost of funds and to the nationally recognized prime lending rate. This approach historically has contributed to a consistent interest rate spread over the long-term and reduces pressure from borrowers to renegotiate loan terms during periods of falling interest rates. Intermountain currently maintains over fifty percent of its loan portfolio in variable interest rate assets.

Additionally, the extent to which borrowers prepay loans is affected by prevailing interest rates. When interest rates increase, borrowers are less likely to prepay loans. When interest rates decrease, borrowers are more likely to prepay loans. Prepayments may affect the levels of loans retained in an institution s portfolio, as well as its net interest income. Intermountain maintains an asset and liability management program intended to manage net interest income through interest rate cycles and to protect its income by controlling its exposure to changing interest rates.

On the liability side, Intermountain seeks to manage its interest rate risk exposure by maintaining a relatively high percentage of non-interest bearing demand deposits, interest-bearing demand deposits and money market accounts. These instruments tend to lag changes in market rates and may afford the bank more protection in increasing interest rate environments, but can also be changed relatively quickly in a declining rate environment. The Bank utilizes various deposit pricing strategies and other borrowing sources to manage its rate risk.

As discussed above, Intermountain uses a simulation model designed to measure the sensitivity of net interest income and net income to changes in interest rates. This simulation model is designed to enable Intermountain to generate a forecast of net interest income and net income given various interest rate forecasts and alternative strategies. The model is also designed to measure the anticipated impact that prepayment risk, basis risk, customer maturity preferences, volumes of new business and changes in the relationship between long-term and short-term interest rates have on the performance of Intermountain. The results of current modeling are within guidelines established by the Company, except that net income falls slightly below the guideline in a 300 basis point downward adjustment in market rates, a scenario that management believes is highly unlikely given current market interest rates. In general, model results reflect marginal performance improvement in the case of a rising rate environment, and a marginal negative impact in a falling rate environment. Given its current asset-sensitivity, Intermountain has implemented certain hedging actions to protect the company s financial performance in a period of falling market interest rates and is evaluating additional protective measures.

Intermountain is continuing to pursue strategies to manage the level of its interest rate risk while increasing its net interest income and net income; 1) through the origination and retention of variable-rate consumer, business banking, construction and commercial real estate loans, which generally have higher yields than residential permanent loans and 2) by increasing the level of its core deposits, which are generally a lower-cost, less rate-sensitive funding source than wholesale borrowings. There can be no assurance that Intermountain will be successful implementing any of these strategies or that, if these strategies are implemented, they will have the intended effect of reducing interest rate risk or increasing net interest income.

Intermountain also uses gap analysis, a traditional analytical tool designed to measure the difference between the amount of interest-earning assets and the amount of interest-bearing liabilities expected to reprice in a given period. Intermountain calculated its one-year cumulative repricing gap position to be negative 41% and a negative 29% at March 31, 2008 and December 31, 2007, respectively. Management attempts to maintain Intermountain s gap position between positive 20% and negative 35%. At March 31, 2008 Intermountain s gap position was outside of the recommended guidelines as the Company intentionally changed to shorter term liability maturities in the current interest rate environment. At December 31, 2007, Intermountain s gap positions were within guidelines established by its Board of Directors. See Results of Operations *Net Interest Income* and Capital Resources.

Liquidity and Sources of Funds

As a financial institution, Intermountain s primary sources of funds from assets include the collection of loan principal and interest payments, cash flows from various securities it invests in, and occasional sales of loans, investments or other assets. Liability financing sources consist primarily of customer deposits, advances from FHLB Seattle and other borrowings. Deposits decreased to $727.1 million at March 31, 2008 from $757.8 million at December 31, 2007, primarily due to decreases in demand accounts, money market accounts and certificates of deposits. The net decrease in deposits was offset on the asset side by decreases in cash, loans receivable and the available for sale investment portfolio. At March 31, 2008 and December 31, 2007, securities sold subject to repurchase agreements and federal funds borrowed were $121.1 million and $124.1 million, respectively. Securities sold subject to repurchase agreements are required to be collateralized by investments with a market value exceeding the face value of the borrowings. Under certain circumstances, Intermountain could be required to pledge additional securities or reduce the borrowings.

During the three months ended March 31, 2008, cash provided by investing activities came from the maturity of investments and the decrease in loans and cash. During the same period, cash used by financing activities consisted primarily of decreases in deposits and borrowings.

Intermountain s credit line with FHLB Seattle provides for borrowings up to a percentage of its total assets subject to general collateralization requirements. At March 31, 2008, the Company s credit line represented a total borrowing capacity of approximately $85.9 million, of which $33.0 million was being utilized through FHLB advances and overnight borrowings. Intermountain also borrows on an unsecured basis from correspondent banks and other financial entities. Correspondent banks and other financial entities provided additional borrowing capacity of $45.1 million at March 31, 2008. As of March 31, 2008 there were no unsecured funds borrowed.

Intermountain actively manages its liquidity to maintain an adequate margin over the level necessary to support expected and potential loan fundings and deposit withdrawals. This is balanced with the need to maximize yield on alternate investments. The liquidity ratio may vary from time to time, depending on economic conditions, savings flows and loan funding needs.

Capital Resources

Intermountain s total stockholders equity was $92.3 million at March 31, 2008 compared with $90.1 million at December 31, 2007. The increase in total stockholders equity was primarily due to the retention of net income in the first quarter of 2008 and the increase in the unrealized gain on the available for sale investment portfolio. Stockholders equity was 9.1% of total assets at March 31, 2008 compared with 8.6% at December 31, 2007.

At March 31, 2008, Intermountain had an unrealized gain of $2.1 million, net of related income taxes, on investments classified as available-for-sale. At December 31, 2007, Intermountain had an unrealized gain of $1.3 million, net of related income taxes, on investments classified as available-for-sale. Fluctuations in prevailing interest rates continue to cause volatility in this component of accumulated comprehensive gain or loss in stockholders equity and may continue to do so in future periods.

Intermountain issued and has outstanding $16.5 million of Trust Preferred Securities. The indenture governing the Trust Preferred Securities limits the ability of Intermountain under certain circumstances to pay dividends or to make other capital distributions. The Trust Preferred Securities are treated as debt of Intermountain.

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These Trust Preferred Securities can be called for redemption beginning in March 2008 by the Company at 100% of the aggregate principal plus accrued and unpaid interest. See Note 3 of Notes to Consolidated Financial Statements.

Intermountain and Panhandle are required by applicable regulations to maintain certain minimum capital levels and ratios of total and Tier 1 capital to risk-weighted assets, and of Tier I capital to average assets. Intermountain and Panhandle plan to maintain their capital resources and regulatory capital ratios through the retention of earnings and the management of the level and mix of assets, although there can be no assurance in this regard. At March 31, 2008, Intermountain exceeded all such regulatory capital requirements and was well-capitalized pursuant to FFIEC regulations.

The following tables set forth the amounts and ratios regarding actual and minimum core Tier 1 risk-based and total risk-based capital requirements, together with the amounts and ratios required in order to meet the definition of a well-capitalized institution as reported on the quarterly FFIEC call report at March 31, 2008.

	Actual		Capital Requirements		Well-Capitalized Requirements	
	Amount	**Ratio**	**Amount**	**Ratio**	**Amount**	**Ratio**
Total capital (to risk-weighted assets):						
The Company	$104,287	11.90%	$70,130	8%	$87,662	10%
Panhandle State Bank	104,767	11.95%	70,131	8%	87,664	10%
Tier I capital (to risk-weighted assets):						
The Company	93,317	10.65%	35,065	4%	52,597	6%
Panhandle State Bank	93,797	10.70%	35,065	4%	52,598	6%
Tier I capital (to average assets)						
The Company	93,317	9.14%	40,833	4%	51,042	5%
Panhandle State Bank	93,797	9.45%	39,713	4%	49,641	5%

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United States. The NDA must include the results of extensive clinical and other testing, as described above, and a compilation of data relating to the product s pharmacology, chemistry, manufacture and controls. In addition, an NDA for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration must contain data assessing the safety and efficacy for the claimed indication in all relevant pediatric subpopulations, and support dosing and administration for each pediatric subpopulation for which the drug is shown to be safe and effective. In some circumstances, the FDA may grant deferrals for the submission of some or all pediatric data, or full or partial waivers. The cost of preparing and submitting an NDA is substantial. Under federal law, NDAs are subject to substantial application user fees and the sponsor of an approved NDA is also subject to annual product and establishment user fees.

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency s threshold determination that the NDA is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. The review process is often significantly extended by FDA requests for additional information or clarification regarding information already provided in the submission. The FDA may also refer applications for novel drug products or drug products that present difficult questions of safety or efficacy to an advisory committee, typically a panel that includes clinicians and other experts, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee. The FDA normally also will conduct a pre-approval inspection to ensure the manufacturing facility, methods and controls are adequate to preserve the drug s identity, strength, quality, purity and stability, and are in compliance with regulations governing cGMPs.

If the FDA evaluation of the NDA and the inspection of manufacturing facilities are favorable, the FDA may issue an approval letter, which authorizes commercial marketing of the drug with specific prescribing information for a specific indication. As a condition of NDA approval, the FDA may require post approval testing, including Phase IV trials, and surveillance to monitor the drug s safety or efficacy and may impose other conditions, including labeling restrictions, which can materially impact the potential market and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Under FDA regulations in effect prior to August 11, 2008, if the NDA did not warrant approval the FDA would instead issue either an approvable letter or a not-approvable letter. Approvable letters generally contained a statement of specific conditions that must be met in order to secure final approval of the NDA. If and when those conditions were met to the FDA s satisfaction, the FDA would typically issue an approval letter. If the FDA s evaluation of the NDA or inspection of the manufacturing facilities was not favorable, the FDA may refuse to approve the NDA or, prior to August 11, 2008, could issue a not-approvable letter. Not-approvable letters outlined the deficiencies in the submission and often required additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately could decide that the application does not satisfy the regulatory criteria for approval.

Under new regulations, effective August 11, 2008, the FDA has discontinued use of approvable and not-approvable letters when taking action on marketing applications. Instead, the FDA now issues a complete response letter to notify a sponsor that the review period for an application is complete and that the application is not ready for approval. A complete response letter describes the deficiencies that the FDA has identified in an application and, when possible, recommends actions that the applicant might take to place the application in condition for approval. Such actions may include, among other things, conducting additional safety or efficacy studies after which the sponsor may resubmit the application for further review. The new regulations also clarify the anticipated additional review time for the FDA to respond to resubmissions, which for significant resubmissions may be six months or longer.

While we believe that any RNAi therapeutic we develop will be regulated as a new drug under the Federal Food, Drug, and Cosmetic Act, the FDA could decide to regulate certain RNAi therapeutic products as biologics under the Public Health Service Act. Biologics must have a biologics license application, or BLA, approved prior to commercialization. Like NDAs, BLAs are subject to user fees. To obtain BLA approval, an applicant must provide non-clinical and clinical evidence and other information to demonstrate that the biologic product is safe, pure and potent, and like NDAs, must complete clinical trials that are typically conducted in three sequential phases (Phase I, II and III). Additionally, the applicant must demonstrate that the facilities in which the product is manufactured, processed, packaged or held meet standards, including cGMPs and any additional standards in the license designed to ensure its continued safety, purity and potency. Biologics establishments are subject to pre-approval inspections. The review process for BLAs is also time consuming and uncertain, and BLA approval may be conditioned on post-approval testing and surveillance. Once granted, BLA approvals may be suspended or revoked under certain circumstances, such as if the product fails to conform to the standards established in the license.

Once an NDA or BLA is approved, a product will be subject to certain post-approval requirements, including requirements for adverse event reporting, submission of periodic reports, recordkeeping, product sampling and distribution. Additionally, the FDA also strictly regulates the promotional claims that may be made about prescription drug products and biologics. In particular, a drug or biologic may not be promoted for uses that are not approved by the FDA as reflected in the product s approved labeling. In addition, the FDA requires substantiation of any claims of superiority of one product over another, including that such claims be proven by adequate and well-controlled head-to-head clinical trials. To the extent that market acceptance of our products may depend on their superiority over existing therapies, any restriction on our ability to advertise or otherwise promote claims of superiority, or requirements to conduct additional expensive clinical trials to provide proof of such claims, could negatively affect the sales of our products or our costs. We must also notify the FDA of any change in an approved product beyond variations already allowed in the approval. Certain changes to the product, its labeling or its manufacturing require prior FDA approval and may require the conduct of further clinical investigations to support the change. Such approvals may be expensive and time-consuming and, if not approved, the FDA will not allow the product to be marketed as modified.

Some of our drug candidates may need to be administered using specialized drug delivery systems. We may rely on drug delivery systems that are already approved to deliver drugs like ours to similar physiological sites or, in some instances, we may need to modify the design or labeling of the legally available device for delivery of our product candidate. In such an event, the FDA may regulate the product as a combination product or require additional approvals or clearances for the modified device. In addition, to the extent the delivery device is owned by another company, we would need that company s cooperation to implement the necessary changes to the device and to obtain any additional approvals or clearances. Obtaining such additional approvals or clearances, and cooperation of other companies, when necessary, could significantly delay, and increase the cost of obtaining marketing approval, which could reduce the commercial viability of a drug candidate. To the extent that we rely on previously unapproved drug delivery systems, we may be subject to additional testing and approval requirements from the FDA above and beyond those described above.

Once an NDA or BLA is approved, the product covered thereby becomes a listed drug that can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA, upon expiration of relevant patents, if any. An approved ANDA provides for marketing of a drug product that has the same active ingredients in the same strength, dosage form and route of administration as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. There is no requirement, other than the requirement for bioequivalence testing, for an ANDA applicant to conduct or submit results of non-clinical or clinical tests to prove the safety or effectiveness of its drug product. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, are listed as such by the FDA and can often be substituted by pharmacists under prescriptions written for the original listed drug.

Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage, dosage form, route of administration or combination, or for a new use, if the FDA deems that the sponsor was required to provide support from new clinical trials to obtain such marketing approval. During such three-year exclusivity period, the FDA cannot grant approval of an ANDA to commercially distribute a generic version of the drug based on that listed drug. However, the FDA can approve generic or other versions of that listed drug, such as a drug that is the same in every way but its indication for use, and thus the value of such exclusivity may be undermined. Federal law also provides a period of up to five years exclusively following approval of a drug containing no previously approved active ingredients, during which ANDAs for generic versions of those drugs cannot be submitted unless the submission accompanies a challenge to a listed patent, in which case the submission may be made four years following the original product approval.

Additionally, in the event that the sponsor of the listed drug has properly informed the FDA of patents covering its listed drug, applicants submitting an ANDA referencing that drug are required to make one of four patent certifications, including certifying that it believes one or more listed patents are invalid or not infringed. If an applicant certifies invalidity or non-infringement, it is required to provide notice of its filing to the NDA sponsor and the patent holder. If the patent holder then initiates a suit for patent infringement against the ANDA sponsor within 45 days of receipt of the notice, the FDA cannot grant effective approval of the ANDA until either 30 months have passed or there has been a court decision holding that the patents in question are invalid, unenforceable or not infringed. If the patent holder does not initiate a suit for patent infringement within the 45 days, the ANDA may be approved immediately upon successful completion of FDA review, unless blocked by a regulatory exclusivity period. If the ANDA applicant certifies that it does not intend to market its generic product before some or all listed patents on the listed drug expire, then the FDA cannot grant effective approval of the ANDA until those patents expire. The first of the ANDA applicants submitting substantially complete applications certifying that one or more listed patents for a particular product are invalid or not infringed may qualify for an exclusivity period of 180 days running from when the generic product is first marketed, during which subsequently submitted ANDAs cannot be granted effective approval. The 180-day generic exclusivity can be forfeited in various ways, including if the first applicant does not market its product within specified statutory timelines. If more than one applicant files a substantially complete ANDA on the same day, each such first applicant will be entitled to share the 180-day exclusivity period, but there will only be one such period, beginning on the date of first marketing by any of the first applicants.

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of drug products. For example, the Food and Drug Administration Amendments Act of 2007, or FDAAA, granted significant new powers to the FDA, many of which are aimed at improving the safety of drug products before and after approval. In particular, the FDAAA authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information, and require risk evaluation and mitigation strategies, or REMS, for certain drugs, including certain currently approved drugs. In addition, it significantly expands the federal government s clinical trial registry and results databank and creates new restrictions on the advertising and promotion of drug products. Under the FDAAA, companies that violate these and other provisions of the law are subject to substantial civil monetary penalties.

In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and development of our product candidates and any products that we may commercialize. It is impossible to predict whether additional legislative changes will be enacted, or FDA regulations, guidance or interpretations changed, or what the impact of any such changes may be.

Foreign Regulation of New Drug Compounds

Approval of a drug or biologic product by comparable regulatory authorities will be necessary in all or most foreign countries prior to the commencement of marketing of the product in those countries, whether or not FDA approval has been obtained. The approval procedure varies among countries and can involve requirements for additional testing. The time required may differ from that required for FDA approval. Although there are some procedures for unified filings in the European Union, in general, each country has its own procedures and requirements, many of which are time consuming and expensive. Thus, there can be substantial delays in obtaining required approvals from foreign regulatory authorities after the relevant applications are filed.

In Europe, marketing authorizations may be submitted under a centralized or decentralized procedure. The centralized procedure is mandatory for the approval of biotechnology and many pharmaceutical products and provides for the grant of a single marketing authorization that is valid in all European Union member states. The decentralized procedure is a mutual recognition procedure that is available at the request of the applicant for medicinal products that are not subject to the centralized procedure. We will strive to choose the appropriate route of European regulatory filing to accomplish the most rapid regulatory approvals. However, our chosen regulatory strategy may not secure regulatory approvals on a timely basis or at all.

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Hazardous Materials

Our research and development processes involve the controlled use of hazardous materials, chemicals and radioactive materials and produce waste products. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products. We do not expect the cost of complying with these laws and regulations to be material.

Manufacturing

We have no commercial manufacturing capabilities. We may manufacture material for use in IND-enabling toxicology studies in animals at our own facility, but we do not anticipate manufacturing the substantial portion of material for human clinical use ourselves. We have contracted with several third-party contract manufacturing organizations for the supply of certain amounts of material to meet our testing needs for pre-clinical toxicology and clinical testing. Commercial quantities of any drugs that we may seek to develop will have to be manufactured in facilities, and by processes, that comply with FDA regulations and other federal, state and local regulations. We plan to rely on third parties to manufacture commercial quantities of any product that we successfully develop. Under our agreement with Isis, at our request, we may negotiate a manufacturing services agreement with Isis for double-stranded RNA products designated to work through an RNAi mechanism.

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Scientific Advisors

We seek advice from our scientific advisory board, which consists of a number of leading scientists and physicians, on scientific and medical matters. Our scientific advisory board meets regularly to assess:

- our research and development programs;
- the design and implementation of our clinical programs;
- our patent and publication strategies;
- new technologies relevant to our research and development programs; and
- specific scientific and technical issues relevant to our business.

The current members of our scientific advisory board are:

Name	Position/Institutional Affiliation
David P. Bartel, Ph.D.	Member/Whitehead Institute for Biomedical Research; Professor/ Massachusetts Institute of Technology
Fritz Eckstein, Ph.D.	Professor/Max Planck Institute
Edward E. Harlow, Ph.D.	Chair/Harvard Medical School
Robert S. Langer, Ph.D.	Institute Professor/Massachusetts Institute of Technology
Judy Lieberman, M.D., Ph.D.	Senior Investigator/Immune Disease Institute Harvard Medical School; Professor/Harvard Medical School
Stephen N. Oesterle, M.D.*	Senior Vice President for Medicine and Technology/Medtronic, Inc.
Paul R. Schimmel, Ph.D.	Ernest and Jean Hahn Professor/Skaggs Institute for Chemical Biology
Phillip A. Sharp, Ph.D.	Institute Professor/The Koch Institute for Integrative Cancer Research, Massachusetts Institute of Technology
Markus Stoffel, M.D., Ph.D.	Professor/Institute of Molecular Systems Biology at the ETH Zurich
Thomas H. Tuschl, Ph.D.	Associate Professor/Rockefeller University
Phillip D. Zamore, Ph.D.	Gretchen Stone Cook Professor/University of Massachusetts Medical School

* Dr. Oesterle participates as an observer on our scientific advisory board.

Employees

As of January 31, 2009, we had 170 employees, 137 of whom were engaged in research and development. None of our employees is represented by a labor union or covered by a collective bargaining agreement, nor have we experienced work stoppages. We believe that relations with our employees are good.

Financial Information About Geographic Areas

See Note 2 to our Consolidated Financial Statements, entitled Segment Information, for financial information about geographic areas. The Notes to our consolidated financial statements are contained herein in Item 8.

Corporate Information

The company comprises four entities, Alnylam Pharmaceuticals, Inc. and three wholly owned subsidiaries (Alnylam U.S., Inc., Alnylam Europe AG and Alnylam Securities Corporation). Alnylam Pharmaceuticals, Inc. is a Delaware corporation that was formed in May 2003. Alnylam U.S., Inc. is also a Delaware corporation that was formed in June 2002. Alnylam Securities Corporation is a Massachusetts corporation that was formed in December 2006. Alnylam Europe AG, which was incorporated in Germany in June 2000 under the name Ribopharma AG, was acquired by Alnylam Pharmaceuticals, Inc. in July 2003. Our principal executive office is located at 300 Third Street, Cambridge, Massachusetts 02142, and our telephone number is (617) 551-8200.

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Investor Information

We maintain an internet website at http://www.alnylam.com. The information on our website is not incorporated by reference into this annual report on Form 10-K and should not be considered to be a part of this annual report on Form 10-K. Our website address is included in this annual report on Form 10-K as an inactive technical reference only. Our reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, including our annual reports on Form 10-K, our quarterly reports on Form 10-Q and our current reports on Form 8-K, and amendments to those reports, are accessible through our website, free of charge, as soon as reasonably practicable after these reports are filed electronically with, or otherwise furnished to, the Securities and Exchange Commission, or SEC. We also make available on our website the charters of our audit committee, compensation committee and nominating and corporate governance committee, our corporate governance guidelines and our code of business conduct and ethics. In addition, we intend to disclose on our web site any amendments to, or waivers from, our code of business conduct and ethics that are required to be disclosed pursuant to the SEC rules.

You may read and copy any materials we file with the SEC at the SEC s Public Reference Room at 100 F Street, NE, Washington, DC 20549. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC also maintains an Internet website that contains reports, proxy and information statements, and other information regarding Alnylam and other issuers that file electronically with the SEC. The SEC s Internet website address is http://www.sec.gov.

Executive Officers of the Registrant

Name	Age	Position
John M. Maraganore, Ph.D.	46	Chief Executive Officer and Director
Barry E. Greene	45	President and Chief Operating Officer
John (Jack) A. Schmidt, Jr., M.D.	58	Senior Vice President and Chief Scientific Officer
Patricia L. Allen	47	Vice President of Finance and Treasurer

John M. Maraganore, Ph.D. has served as our Chief Executive Officer and as a member of our board of directors since December 2002. Dr. Maraganore also served as our President from December 2002 to December 2007. From April 2000 to December 2002, Dr. Maraganore served as Senior Vice President, Strategic Product Development at Millennium Pharmaceuticals, Inc., a biopharmaceutical company. Dr. Maraganore serves as a member of the board of directors of the Biotechnology Industry Organization.

Barry E. Greene has served as our President and Chief Operating Officer since December 2007, as our Chief Operating Officer since he joined us in October 2003, and from February 2004 through December 2005, as our Treasurer. From February 2001 to September 2003, Mr. Greene served as General Manager of Oncology at Millennium Pharmaceuticals, Inc., a biopharmaceutical company. Mr. Greene serves as a member of the board of directors of Acorda Therapeutics, Inc., a biotechnology company.

John (Jack) A. Schmidt, Jr., M.D. has served as our Senior Vice President and Chief Scientific Officer since he joined us in September 2008. From August 2004 to September 2008, Dr. Schmidt served as Vice President and Associate Director, Discovery Research and a U.S. member of the Sanofi-aventis Global Discovery Leadership Team where he was also responsible for initiatives in biotherapeutics, external innovation, and discovery initiatives in China. From 2000 to 2004, he served as Vice President and Head of the Respiratory and Rheumatoid Arthritis Disease Group at Aventis.

Patricia L. Allen has served as our Vice President of Finance since she joined us in May 2004, and as our Treasurer since January 2006. From March 1992 to May 2004, Ms. Allen held various positions at Alkermes, Inc., a biopharmaceutical company, most recently as Director of Finance. Ms. Allen is a certified public accountant.

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ITEM 1A. RISK FACTORS.

Our business is subject to numerous risks. We caution you that the following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in filings with the SEC, press releases, communications with investors and oral statements. Any or all of our forward-looking statements in this annual report on Form 10-K and in any other public statements we make may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in the discussion below will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially from those anticipated in forward-looking statements. We explicitly disclaim any obligation to update any forward-looking statements to reflect events or circumstances that arise after the date hereof. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC.

Risks Related to Our Business

Risks Related to Being an Early Stage Company

Because we have a short operating history, there is a limited amount of information about us upon which you can evaluate our business and prospects.

Our operations began in 2002 and we have only a limited operating history upon which you can evaluate our business and prospects. In addition, as an early-stage company, we have limited experience and have not yet demonstrated an ability to successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields, particularly in the biopharmaceutical area. For example, to execute our business plan, we will need to successfully:

- execute product development activities using unproven technologies related to both RNAi and to the delivery of siRNAs to the relevant cell tissue;
- build and maintain a strong intellectual property portfolio;
- gain acceptance for the development of our product candidates and any products we commercialize;
- develop and maintain successful strategic alliances; and
- manage our spending as costs and expenses increase due to clinical trials, regulatory approvals and commercialization.

If we are unsuccessful in accomplishing these objectives, we may not be able to develop product candidates, commercialize products, raise capital, expand our business or continue our operations.

The approach we are taking to discover and develop novel RNAi therapeutics is unproven and may never lead to marketable products.

We have concentrated our efforts and therapeutic product research on RNAi technology, and our future success depends on the successful development of this technology and products based on it. Neither we nor any other company has received regulatory approval to market therapeutics utilizing siRNAs, the class of molecule we are trying to develop into drugs. The scientific discoveries that form the basis for our efforts to discover and develop new drugs are relatively new. The scientific evidence to support the feasibility of developing drugs based on these discoveries is both preliminary and limited. Skepticism as to the feasibility of developing RNAi therapeutics has been expressed in scientific literature. For example, there are potential challenges to achieving safe RNAi therapeutics based on the so-called off-target effects and activation of the interferon response.

Relatively few drug candidates based on these discoveries have ever been tested in animals or humans. siRNAs may not naturally possess the inherent properties typically required of drugs, such as the ability to be stable in the body long enough to reach the tissues in which their effects are required, nor the ability to enter cells within these tissues in order to exert their effects. We currently have only limited data, and no conclusive evidence, to suggest that we can introduce these drug-like properties into siRNAs. We may spend large amounts of money trying to introduce these properties, and may never succeed in doing so. In addition, these compounds may not demonstrate in patients the chemical and pharmacological properties ascribed to them in laboratory studies, and they may interact with human biological systems in unforeseen, ineffective or harmful ways. As a result, we may never succeed in developing a marketable product. If we do not successfully develop and commercialize drugs based upon our technological approach, we may not become profitable and the value of our common stock will decline.

Further, our focus solely on RNAi technology for developing drugs, as opposed to multiple, more proven technologies for drug development, increases the risks associated with the ownership of our common stock. If we are not successful in developing a product candidate using RNAi technology, we may be required to change the scope and direction of our product development activities. In that case, we may not be able to identify and implement successfully an alternative product development strategy.

Risks Related to Our Financial Results and Need for Financing

We have a history of losses and may never be profitable.

We have experienced significant operating losses since our inception. As of December 31, 2008, we had an accumulated deficit of $252.2 million. To date, we have not developed any products nor generated any revenues from the sale of products. Further, we do not expect to generate any such revenues in the foreseeable future. We expect to continue to incur annual net operating losses over the next several years and will require substantial resources over the next several years as we expand our efforts to discover, develop and commercialize RNAi therapeutics. We anticipate that the majority of any revenue we generate over the next several years will be from alliances with pharmaceutical companies or funding from contracts with the government, but cannot be certain that we will be able to secure or maintain these alliances or contracts, or meet the obligations or achieve any milestones that we may be required to meet or achieve to receive payments.

To become and remain consistently profitable, we must succeed in discovering, developing and commercializing novel drugs with significant market potential. This will require us to be successful in a range of challenging activities, including pre-clinical testing and clinical trial stages of development, obtaining regulatory approval for these novel drugs and manufacturing, marketing and selling them. We may never succeed in these activities, and may never generate revenues that are significant enough to achieve profitability. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. If we cannot become and remain consistently profitable, the market price of our common stock could decline. In addition, we may be unable to raise capital, expand our business, diversify our product offerings or continue our operations.

We will require substantial additional funds to complete our research and development activities and if additional funds are not available, we may need to critically limit, significantly scale back or cease our operations.

We have used substantial funds to develop our RNAi technologies and will require substantial funds to conduct further research and development, including pre-clinical testing and clinical trials of any product candidates, and to manufacture and market any products that are approved for commercial sale. Because the successful development of our products is uncertain, we are unable to estimate the actual funds we will require to develop and commercialize them.

Our future capital requirements and the period for which we expect our existing resources to support our operations may vary from what we expect. We have based our expectations on a number of factors, many of which are difficult to predict or are outside of our control, including:

- our progress in demonstrating that siRNAs can be active as drugs;

our ability to develop relatively standard procedures for selecting and modifying siRNA drug candidates;

progress in our research and development programs, as well as the magnitude of these programs;

the timing, receipt and amount of milestone and other payments, if any, from present and future collaborators, if any;

the timing, receipt and amount of funding under current and future government contracts, if any;

our ability to maintain and establish additional collaborative arrangements;

the resources, time and costs required to initiate and complete our pre-clinical and clinical trials, obtain regulatory approvals, protect our intellectual property and obtain and maintain licenses to third-party intellectual property;

the cost of preparing, filing, prosecuting, maintaining and enforcing patent claims;

progress in the research and development programs of Regulus Therapeutics; and

the timing, receipt and amount of sales and royalties, if any, from our potential products.

If our estimates and predictions relating to these factors are incorrect, we may need to modify our operating plan.

We will be required to seek additional funding in the future and intend to do so through either collaborative arrangements, public or private equity offerings or debt financings, or a combination of one or more of these funding sources. Additional funds may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our stockholders will result. In addition, our investor rights agreement with Novartis provides Novartis with the right generally to maintain its ownership percentage in us and our common stock purchase agreement with Roche contains a similar provision. In May 2008, Novartis purchased 213,888 shares of our common stock at a purchase price of $25.29 per share, which resulted in a 0.5% increase in Novartis ownership position. At December 31, 2008, Novartis ownership position was 13.2%. While the exercise of these rights by Novartis provided us with $5.4 million in cash, and the exercise in the future by Novartis or Roche may provide us with additional funding under some circumstances, this exercise and any future exercise of these rights by Novartis or Roche will also cause further dilution to our stockholders. Debt financing, if available, may involve restrictive covenants that could limit our flexibility in conducting future business activities. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies, product candidates or products that we would otherwise pursue on our own.

If the estimates we make, or the assumptions on which we rely, in preparing our consolidated financial statements prove inaccurate, our actual results may vary from those reflected in our projections and accruals.

Our consolidated financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct.

The investment of our cash balance and our investments in marketable debt securities are subject to risks which may cause losses and affect the liquidity of these investments.

At December 31, 2008, we had $512.7 million in cash, cash equivalents and marketable securities. We historically have invested these amounts in corporate bonds, commercial paper, securities issued by the U.S. government, certificates of deposit and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. These investments are subject to general credit, liquidity, market and interest rate risks, which may be affected by U.S. sub-prime mortgage defaults that have affected various sectors of the financial markets and caused credit and liquidity issues. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our consolidated financial statements. In addition, should our investments cease paying or reduce the amount of interest paid to us,

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our interest income would suffer. For example, due to recent market conditions, interest rates have fallen, and accordingly, despite a higher average cash balance in 2008, our interest income decreased to $14.4 million in 2008 from $15.4 million in 2007. These market risks associated with our investment portfolio may have a negative adverse effect on our results of operations, liquidity and financial condition.

Risks Related to Our Dependence on Third Parties

Our collaboration with Novartis is important to our business. If this collaboration is unsuccessful, Novartis terminates this collaboration or this collaboration results in competition between us and Novartis for the development of drugs targeting the same diseases, our business could be adversely affected.

In October 2005, we entered into a collaboration agreement with Novartis. Under this agreement, Novartis can select up to 30 exclusive targets to include in the collaboration, which number may be increased to 40 under certain circumstances and upon additional payments. Novartis pays the costs to develop these drug candidates and will commercialize and market any products derived from this collaboration. For RNAi therapeutic products successfully developed under the agreement, if any, we would be entitled to receive milestone payments upon achievement of certain specified development and annual net sales events, up to an aggregate of $75.0 million per therapeutic product, as well as royalties on the annual net sales, if any. The Novartis agreement has an initial term of three years, with the option for two additional one-year extensions at the election of Novartis. In July 2008, Novartis elected to extend the initial term for an additional year, through October 2009. Novartis retains the right to extend the term for a second additional year, which right must be exercised no later than July 2009. Novartis may elect to terminate this collaboration in the event of a material uncured breach by us. We expect that a substantial amount of funding will come from this collaboration. If this collaboration is unsuccessful, or if it is terminated, our business could be adversely affected.

This agreement also provides Novartis with a non-exclusive option to integrate into its operations our intellectual property relating to RNAi technology, excluding any technology related to delivery of nucleic acid based molecules. Novartis may exercise this integration option at any point during the research term, as defined in the collaboration and license agreement. The research term expires in October 2009 and may be extended until October 2010 at Novartis election. The license grant under the integration option, if exercised, would be structured similarly to our non-exclusive platform licenses with Roche and Takeda. If Novartis elects to exercise this option, Novartis could become a competitor of ours in the development of RNAi-based drugs targeting the same diseases. Novartis has significantly greater financial resources and far more experience than we do in developing and marketing drugs, which could put us at a competitive disadvantage if we were to compete with Novartis in the development of RNAi-based drugs targeting the same disease. Accordingly, the exercise by Novartis of this option could adversely affect our business.

Our agreement with Novartis allows us to continue to develop products on an exclusive basis on our own with respect to targets not selected by Novartis for inclusion in the collaboration. We may need to form additional alliances to develop products. However, our agreement with Novartis provides Novartis with a right of first offer, for a defined term, in the event that we propose to enter into an agreement with a third party with respect to such targets. This right of first offer may make it difficult for us to form future alliances around specific targets with other parties.

Our license and collaboration agreements with Roche and Takeda are important to our business. If Roche and/or Takeda do not successfully develop drugs pursuant to these agreements or these agreements result in competition between us and Roche and/or Takeda for the development of drugs targeting the same diseases, our business could be adversely affected.

In July 2007, we entered into a license and collaboration agreement with Roche. Under the license and collaboration agreement we granted Roche a non-exclusive license to our intellectual property to develop and commercialize therapeutic products that function through RNAi, subject to our existing contractual obligations to third parties. The license is limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases and may be expanded to include up to 18 additional therapeutic areas, comprising all other fields of human disease, as identified and agreed upon by the parties, upon payment to us by Roche of an additional

$50.0 million for each additional therapeutic area, if any. In addition, in exchange for our contributions under the collaboration agreement, for each RNAi therapeutic product successfully developed by Roche, its affiliates, or sublicensees under the collaboration agreement, if any, we are entitled to receive milestone payments upon achievement of specified development and sales events, totaling up to an aggregate of $100.0 million per therapeutic target, together with royalty payments based on worldwide annual net sales, if any. In May 2008, we entered into a similar license and collaboration agreement with Takeda, which is limited to the therapeutic areas of oncology and metabolic diseases, and which may be expanded to include up to 20 additional therapeutic areas, comprising all other fields of human disease, as identified and agreed upon by the parties, upon payment to us by Takeda of an additional $50.0 million for each additional therapeutic area, if any. For each RNAi therapeutic product successfully developed by Takeda, its affiliates and sublicensees, if any, we are entitled to receive specified development and commercialization milestones, totaling up to $171.0 million per product, together with royalty payments based on worldwide annual net sales, if any. In addition, we have agreed that for a period of five years, we will not grant any other party rights to develop RNAi therapeutics in the Asian territory.

If Roche or Takeda fails to successfully develop products using our technology, we may not receive any milestone or royalty payments under these agreements. In addition, even if Takeda is not successful in its efforts, for a period of five years we will be limited in our ability to form alliances with other parties in the Asia territory. We also have the option under the Takeda agreement, exercisable until the start of Phase III development, to opt-in under a 50-50 profit sharing agreement to the development and commercialization in the United States of up to four Takeda licensed products, and would be entitled to opt-in rights for two additional products for each additional field expansion, if any, elected by Takeda under the collaboration agreement. If Takeda fails to successfully develop products, we may not realize any economic benefit from these opt-in rights.

Finally, either Roche or Takeda could become a competitor of ours in the development of RNAi-based drugs targeting the same diseases. Each of these companies has significantly greater financial resources than we do and has far more experience in developing and marketing drugs, which could put us at a competitive disadvantage if we were to compete with either Roche or Takeda in the development of RNAi-based drugs targeting the same disease.

We may not be able to execute our business strategy if we are unable to enter into alliances with other companies that can provide business and scientific capabilities and funds for the development and commercialization of our drug candidates. If we are unsuccessful in forming or maintaining these alliances on favorable terms, our business may not succeed.

We do not have any capability for sales, marketing or distribution and have limited capabilities for drug development. In addition, we believe that other companies are expending substantial resources in developing safe and effective means of delivering siRNAs to relevant cell and tissue types. Accordingly, we have entered into alliances with other companies and collaborators that we believe can provide such capabilities, and we intend to enter into additional alliances in the future. For example, we intend to enter into (1) non-exclusive platform alliances which will enable our collaborators to develop RNAi therapeutics and will bring in additional funding with which we can develop our RNAi therapeutics, and (2) alliances to jointly develop specific drug candidates and to jointly commercialize RNAi therapeutics, if they are approved, and/or ex-U.S. market geographic partnerships on specific RNAi therapeutic programs. In such alliances, we may expect our collaborators to provide substantial capabilities in delivery of RNAi therapeutics to the relevant cell or tissue type, clinical development, regulatory affairs, and/or marketing, sales and distribution. For example, under our collaboration with Medtronic, we are jointly developing ALN-HTT, an RNAi therapeutic for Huntington s disease, which would be delivered using an implanted infusion device developed by Medtronic. The success of this collaboration will depend, in part, on Medtronic s expertise in the area of delivery by infusion device. In other alliances, we may expect our collaborators to develop, market and sell certain of our product candidates. We may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties. For example, we will jointly develop and commercialize products for RSV in partnership with Cubist in North America. We will rely entirely on Cubist for the development and commercialization of products for RSV in the rest of the world outside of Asia, where we will rely on Kyowa Hakko for development and commercialization of products for RSV. If Cubist and Kyowa Hakko are not successful in their commercialization efforts, our future revenues for RSV may be adversely affected.

We may not be successful in entering into such alliances on favorable terms due to various factors, including Novartis right of first offer on our drug targets. Even if we do succeed in securing such alliances, we may not be able to maintain them if, for example, development or approval of a drug candidate is delayed or sales of an approved drug are disappointing. Furthermore, any delay in entering into collaboration agreements could delay the development and commercialization of our drug candidates and reduce their competitiveness even if they reach the market. Any such delay related to our collaborations could adversely affect our business.

For certain drug candidates that we may develop, we have formed collaborations to fund all or part of the costs of drug development and commercialization, such as our collaborations with Novartis, as well as collaborations with Cubist, Medtronic and NIAID. We may not, however, be able to enter into additional collaborations, and the terms of any collaboration agreement we do secure may not be favorable to us. If we are not successful in our efforts to enter into future collaboration arrangements with respect to a particular drug candidate, we may not have sufficient funds to develop that or any other drug candidate internally, or to bring any drug candidates to market. If we do not have sufficient funds to develop and bring our drug candidates to market, we will not be able to generate sales revenues from these drug candidates, and this will substantially harm our business.

If any collaborator terminates or fails to perform its obligations under agreements with us, the development and commercialization of our drug candidates could be delayed or terminated.

Our dependence on collaborators for capabilities and funding means that our business could be adversely affected if any collaborator terminates its collaboration agreement with us or fails to perform its obligations under that agreement. Our current or future collaborations, if any, may not be scientifically or commercially successful. Disputes may arise in the future with respect to the ownership of rights to technology or products developed with collaborators, which could have an adverse effect on our ability to develop and commercialize any affected product candidate.

Our current collaborations allow, and we expect that any future collaborations will allow, either party to terminate the collaboration for a material breach by the other party. Our agreement with Kyowa Hakko for the development and commercialization of ALN-RSV01 for the treatment of RSV infection in Japan and other major markets in Asia may be terminated by Kyowa Hakko without cause upon 180-days prior written notice to us, subject to certain conditions, and our agreement with Cubist relating to the development and commercialization of RSV therapeutics in territories outside of Asia may be terminated by Cubist at any time upon as little as three months prior written notice, if such notice is given prior to the acceptance for filing of the first application for regulatory approval of a licensed product. If we were to lose a commercialization collaborator, we would have to attract a new collaborator or develop internal sales, distribution and marketing capabilities, which would require us to invest significant amounts of financial and management resources.

In addition, if a collaborator terminates its collaboration with us, for breach or otherwise, it would be difficult for us to attract new collaborators and could adversely affect how we are perceived in the business and financial communities. A collaborator, or in the event of a change in control of a collaborator, the successor entity, could determine that it is in its financial interest to:

- pursue alternative technologies or develop alternative products, either on its own or jointly with others, that may be competitive with the products on which it is collaborating with us or which could affect its commitment to the collaboration with us;

- pursue higher-priority programs or change the focus of its development programs, which could affect the collaborator s commitment to us; or if it has marketing rights, choose to devote fewer resources to the marketing of our product candidates, if any are approved for marketing, than it does for product candidates developed without us.

If any of these occur, the development and commercialization of one or more drug candidates could be delayed, curtailed or terminated because we may not have sufficient financial resources or capabilities to continue such development and commercialization on our own.

We depend on government contracts to partially fund our research and development efforts and may enter into additional government contracts in the future. If current or future government funding, if any, is reduced or delayed, our drug development efforts for such funded programs may be negatively affected.

In September 2006, NIAID awarded us a contract for up to $23.0 million over four years to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus, including the Ebola virus. Of the $23.0 million in funding, the government initially committed to pay us up to $14.2 million over the first two years of the contract. In June 2008, as a result of the progress of the program, the government awarded us an additional $7.5 million, to be paid through September 2009 for the third year of the contract, together with any remaining funds carried over from the funding allocated for the first two years of the contract. We cannot be certain that the government will appropriate the funds necessary for this contract in future budgets. In addition, the government can terminate the agreement in specified circumstances. If we do not receive the $23.0 million we expect to receive under this contract, we may not be able to develop therapeutics to treat Ebola.

For example, in August 2007, DTRA awarded us a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus infection. When granted, this federal contract provided for potential funding of up to $38.6 million through February 2011. Of this amount, the government initially committed to pay us up to $10.9 million through February 2009, which term includes a six-month extension granted by DTRA in July 2008. However, following a program review in early 2009, we and DTRA have determined to end this program and accordingly, the remaining funds will not be accessed.

Regulus Therapeutics is important to our business. If Regulus Therapeutics does not successfully develop drugs pursuant to this license and collaboration agreement or Regulus Therapeutics is sold to Isis or a third-party, our business could be adversely affected.

In September 2007, we and Isis formed Regulus Therapeutics, of which we own 49%, to discover, develop and commercialize microRNA-based therapeutics. Regulus Therapeutics intends to address therapeutic opportunities that arise from abnormal expression or mutations in microRNAs. Generally, we do not have rights to pursue microRNA-based therapeutics independently of Regulus Therapeutics. If Regulus Therapeutics is unable to discover, develop and commercialize microRNA-based therapeutics, our business could be adversely affected.

In addition, subject to certain conditions, we and Isis each have the right to initiate a buy-out of Regulus Therapeutics assets, including Regulus Therapeutics intellectual property and rights to licensed intellectual property. Following the initiation of such a buy-out, we and Isis will mutually determine whether to sell Regulus Therapeutics to us, Isis or a third party. We may not have sufficient funds to buy out Isis interest in Regulus Therapeutics and we may not be able to obtain the financing to do so. In addition, Isis may not be willing to sell their interest in Regulus Therapeutics. If Regulus Therapeutics is sold to Isis or a third party, we may lose our rights to participate in the development and commercialization of microRNA-based therapeutics. If we and Isis are unable to negotiate a sale of Regulus Therapeutics, Regulus Therapeutics will distribute and assign its rights, interests and assets to us and Isis in accordance with our percentage interests, except for Regulus Therapeutics intellectual property and license rights, to which each of us and Isis will receive co-exclusive rights, subject to certain specified exceptions. In this event, we could face competition from Isis in the development of microRNA-based therapeutics.

We have very limited manufacturing experience or resources and we must incur significant costs to develop this expertise or rely on third parties to manufacture our products.

We have very limited manufacturing experience. Our internal manufacturing capabilities are limited to small-scale production of non-good manufacturing practice material for use in *in vitro* and *in vivo* experiments. Our products utilize specialized formulations, such as liposomes, whose scale-up and manufacturing could be very difficult. We also have very limited experience in such scale-up and manufacturing, requiring us to depend on third parties, who might not be able to deliver in a timely manner, or at all. In order to develop products, apply for regulatory approvals and commercialize our products, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. We may manufacture clinical trial materials ourselves or we may rely on others to manufacture the materials we will require for any clinical trials that we initiate. Only a limited number of manufacturers supply synthetic siRNAs. We currently rely on several contract manufacturers for our supply of

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synthetic siRNAs. There are risks inherent in pharmaceutical manufacturing that could affect the ability of our contract manufacturers to meet our delivery time requirements or provide adequate amounts of material to meet our needs. Included in these risks are synthesis and purification failures and contamination during the manufacturing process, which could result in unusable product and cause delays in our development process, as well as additional expense to us. To fulfill our siRNA requirements, we may also need to secure alternative suppliers of synthetic siRNAs. In addition to the manufacture of the synthetic siRNAs, we may have additional manufacturing requirements related to the technology required to deliver the siRNA to the relevant cell or tissue type. In some cases, the delivery technology we utilize is highly specialized or proprietary, and for technical and legal reasons, we may have access to only one or a limited number of potential manufacturers for such delivery technology. Failure by these manufacturers to properly formulate our siRNAs for delivery could also result in unusable product and cause delays in our discovery and development process, as well as additional expense to us.

The manufacturing process for any products that we may develop is subject to the FDA and foreign regulatory authority approval process and we will need to contract with manufacturers who can meet all applicable FDA and foreign regulatory authority requirements on an ongoing basis. In addition, if we receive the necessary regulatory approval for any product candidate, we also expect to rely on third parties, including our commercial collaborators, to produce materials required for commercial supply. We may experience difficulty in obtaining adequate manufacturing capacity for our needs. If we are unable to obtain or maintain contract manufacturing for these product candidates, or to do so on commercially reasonable terms, we may not be able to successfully develop and commercialize our products.

To the extent that we enter into manufacturing arrangements with third parties, we will depend on these third parties to perform their obligations in a timely manner and consistent with regulatory requirements, including those related to quality control and quality assurance. The failure of a third-party manufacturer to perform its obligations as expected could adversely affect our business in a number of ways, including:

- we may not be able to initiate or continue clinical trials of products that are under development;
- we may be delayed in submitting regulatory applications, or receiving regulatory approvals, for our products candidates;
- we may lose the cooperation of our collaborators;
- we may be required to cease distribution or recall some or all batches of our products; and
- ultimately, we may not be able to meet commercial demands for our products.

If a third-party manufacturer with whom we contract fails to perform its obligations, we may be forced to manufacture the materials ourselves, for which we may not have the capabilities or resources, or enter into an agreement with a different third-party manufacturer, which we may not be able to do with reasonable terms, if at all. In some cases, the technical skills required to manufacture our product may be unique to the original manufacturer and we may have difficulty transferring such skills to a back-up nor alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. Furthermore, a manufacturer may possess technology related to the manufacture of our product candidate that such manufacturer owns independently. This would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our products.

We have no sales, marketing or distribution experience and would have to invest significant financial and management resources to establish these capabilities.

We have no sales, marketing or distribution experience. We currently expect to rely heavily on third parties to launch and market certain of our product candidates, if approved. However, if we elect to develop internal sales, distribution and marketing capabilities, we will need to invest significant financial and management resources. For products where we decide to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including:

- we may not be able to attract and build a significant marketing or sales force;
- the cost of establishing a marketing or sales force may not be justifiable in light of the revenues generated by any particular product; and
- our direct sales and marketing efforts may not be successful.

If we are unable to develop our own sales, marketing and distribution capabilities, we will not be able to successfully commercialize our products without reliance on third parties.

The current credit and financial market conditions may exacerbate certain risks affecting our business.

Due to the recent tightening of global credit, there may be a disruption or delay in the performance of our third-party contractors, suppliers or collaborators. We rely on third parties for several important aspects of our business, including significant portions of our manufacturing needs, development of product candidates and conduct of clinical trials. If such third parties are unable to satisfy their commitments to us, our business could be adversely affected.

Risks Related to Managing Our Operations

If we are unable to attract and retain qualified key management and scientists, staff consultants and advisors, our ability to implement our business plan may be adversely affected.

We are highly dependent upon our senior management and scientific staff. The loss of the service of any of the members of our senior management, including Dr. John Maraganore, our Chief Executive Officer, may significantly delay or prevent the achievement of product development and other business objectives. Our employment agreements with our key personnel are terminable without notice. We do not carry key man life insurance on any of our employees.

Although we have generally been successful in our recruiting efforts, as well as our retention of employees, we face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions, many of which have substantially greater resources with which to reward qualified individuals than we do. We may be unable to attract and retain suitably qualified individuals, and our failure to do so could have an adverse effect on our ability to implement our business plan.

We may have difficulty managing our growth and expanding our operations successfully as we seek to evolve from a company primarily involved in discovery and pre-clinical testing into one that develops and commercializes drugs.

Since we commenced operations in 2002, we have grown substantially. As of December 31, 2008, we had approximately 164 employees in our facility in Cambridge, Massachusetts. Our rapid and substantial growth may place a strain on our administrative and operational infrastructure. If drug candidates we develop enter and advance through clinical trials, we will need to expand our development, regulatory, manufacturing, marketing and sales capabilities or contract with other organizations to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various collaborators, suppliers and other organizations. Our ability to manage our operations and growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

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Risks Related to Our Industry

Risks Related to Development, Clinical Testing and Regulatory Approval of Our Drug Candidates

Any drug candidates we develop may fail in development or be delayed to a point where they do not become commercially viable.

Pre-clinical testing and clinical trials of new drug candidates are lengthy and expensive and the historical failure rate for drug candidates is high. We are developing our most advanced product candidate, ALN-RSV01, for the treatment of RSV infection. In January 2008, we completed our GEMINI study, a Phase II trial designed to evaluate the safety, tolerability and anti-viral activity of ALN-RSV01 in adult subjects experimentally infected with RSV. We commenced a second Phase II trial in April 2008 to assess the safety and tolerability of ALN-RSV01 in adult lung transplant patients naturally infected with RSV and we intend to continue the clinical development of ALN-RSV01. In addition, in December 2008, we submitted an IND to the FDA for ALN-VSP, our first systemically delivered RNAi therapeutic. We are developing ALN-VSP for the treatment of certain liver cancers. We received clearance from the FDA in January 2009 to proceed with a Phase I study. However, we may not be able to further advance these or any other product candidate through clinical trials. If we successfully enter into clinical studies, the results from pre-clinical testing or early clinical trials of a drug candidate may not predict the results that will be obtained in subsequent human clinical trials. For example, ALN-VSP and our other systemically delivered therapeutic candidates employ novel delivery formulations that have yet to be evaluated in human studies and have yet to be proven safe and effective in clinical trials. We, the FDA or other applicable regulatory authorities, or an institutional review board, or IRB, may suspend clinical trials of a drug candidate at any time for various reasons, including if we or they believe the subjects or patients participating in such trials are being exposed to unacceptable health risks. Among other reasons, adverse side effects of a drug candidate on subjects or patients in a clinical trial could result in the FDA or foreign regulatory authorities suspending or terminating the trial and refusing to approve a particular drug candidate for any or all indications of use.

Clinical trials of a new drug candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the drug candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the age and condition of the patients, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, the seasonality of infections and the eligibility criteria for the clinical trial. Delays in patient enrollment can result in increased costs and longer development times.

Clinical trials also require the review and oversight of IRBs, which approve and continually review clinical investigations and protect the rights and welfare of human subjects. Inability to obtain or delay in obtaining IRB approval can prevent or delay the initiation and completion of clinical trials, and the FDA may decide not to consider any data or information derived from a clinical investigation not subject to initial and continuing IRB review and approval in support of a marketing application.

Our drug candidates that we develop may encounter problems during clinical trials that will cause us, an IRB or regulatory authorities to delay, suspend or terminate these trials, or that will delay the analysis of data from these trials. If we experience any such problems, we may not have the financial resources to continue development of the drug candidate that is affected, or development of any of our other drug candidates. We may also lose, or be unable to enter into, collaborative arrangements for the affected drug candidate and for other drug candidates we are developing.

Delays in clinical trials could reduce the commercial viability of our drug candidates. Any of the following could, among other things, delay our clinical trials:

delays in filing initial drug applications;

conditions imposed on us by the FDA or comparable foreign authorities regarding the scope or design of our clinical trials;

problems in engaging IRBs to oversee trials or problems in obtaining or maintaining IRB approval of trials;

delays in enrolling patients and volunteers into clinical trials;

high drop-out rates for patients and volunteers in clinical trials;

negative or inconclusive results from our clinical trials or the clinical trials of others for drug candidates similar to ours;

inadequate supply or quality of drug candidate materials or other materials necessary for the conduct of our clinical trials;

serious and unexpected drug-related side effects experienced by participants in our clinical trials or by individuals using drugs similar to our product candidates; or

unfavorable FDA or other regulatory agency inspection and review of a clinical trial site or records of any clinical or pre-clinical investigation.

Even if we successfully complete clinical trials of our drug candidates, any given drug candidate may not prove to be an effective treatment for the diseases for which it was being tested.

The FDA approval process may be delayed for any drugs we develop that require the use of specialized drug delivery devices.

Some drug candidates that we develop may need to be administered using specialized drug delivery devices that deliver RNAi therapeutics directly to diseased parts of the body. For example, we believe that product candidates we develop for Parkinson s disease, HD or other central nervous system diseases may need to be administered using such a device. For neurodegenerative diseases, we have entered into a collaboration agreement with Medtronic to pursue potential development of drug-device combinations incorporating RNAi therapeutics. We may not achieve successful development results under this collaboration and may need to seek other collaboration partners to develop alternative drug delivery systems, or utilize existing drug delivery systems, for the direct delivery of RNAi therapeutics for these diseases. While we expect to rely on drug delivery systems that have been approved by the FDA or other regulatory agencies to deliver drugs like ours to similar physiological sites, we, or our collaborator, may need to modify the design or labeling of such delivery device for some products we may develop. In such an event, the FDA may regulate the product as a combination product or require additional approvals or clearances for the modified delivery device. Further, to the extent the specialized delivery device is owned by another company, we would need that company s cooperation to implement the necessary changes to the device, or its labeling, and to obtain any additional approvals or clearances. In cases where we do not have an ongoing collaboration with the company that makes the device, obtaining such additional approvals or clearances and the cooperation of such other company could significantly delay and increase the cost of obtaining marketing approval, which could reduce the commercial viability of our drug candidate. In summary, we may be unable to find, or experience delays in finding, suitable drug delivery systems to administer RNAi therapeutics directly to diseased parts of the body, which could negatively affect our ability to successfully commercialize these RNAi therapeutics.

We may be unable to obtain United States or foreign regulatory approval and, as a result, be unable to commercialize our drug candidates.

Our drug candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, recordkeeping, labeling, marketing and distribution of drugs. Rigorous pre-clinical testing and clinical trials and an extensive regulatory approval process are required to be successfully completed in the United States and in many foreign jurisdictions before a new drug can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the drug candidates we may develop will obtain the appropriate regulatory approvals necessary for us or our collaborators to begin selling them.

We have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. The time required to obtain FDA and other approvals is unpredictable but typically takes many years following the commencement of clinical trials, depending upon the complexity of the drug candidate. Any analysis we perform of data from pre-clinical and clinical activities is subject to confirmation and interpretation by regulatory authorities, which could delay, limit or prevent regulatory approval. We may also encounter unexpected delays or increased costs due to new government regulations, for example, from future legislation or administrative action, or from changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. For example, the Food and Drug Administration Amendments Act of 2007, or FDAAA, may make it more difficult and costly for us to obtain regulatory approval of our product candidates and to produce, market and distribute products after approval. The FDAAA granted a variety of new powers to the FDA, many of which are aimed at improving the safety of drug products before and after approval. In particular, it authorizes the FDA to, among other things, require post-approval studies and clinical trials, mandate changes to drug labeling to reflect new safety information, and require risk evaluation and mitigation strategies, or REMS, for certain drugs, including certain currently approved drugs. In addition, it significantly expanded the federal government s clinical trial registry and results databank and creates new restrictions on the advertising and promotion of drug products. Under the FDAAA, companies that violate the new law are subject to substantial civil monetary penalties.

Because the drugs we are intending to develop may represent a new class of drug, the FDA has not yet established any definitive policies, practices or guidelines in relation to these drugs. While the product candidates that we are currently developing are regulated as a new drug under the Federal Food, Drug, and Cosmetic Act, the FDA could decide to regulate them or other products we may develop as biologics under the Public Health Service Act. The lack of policies, practices or guidelines may hinder or slow review by the FDA of any regulatory filings that we may submit. Moreover, the FDA may respond to these submissions by defining requirements we may not have anticipated. Such responses could lead to significant delays in the clinical development of our product candidates. In addition, because there may be approved treatments for some of the diseases for which we may seek approval, in order to receive regulatory approval, we will need to demonstrate through clinical trials that the product candidates we develop to treat these diseases, if any, are not only safe and effective, but safer or more effective than existing products. Furthermore, in recent years, there has been increased public and political pressure on the FDA with respect to the approval process for new drugs, and the number of approvals to market new drugs has declined.

Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular drug candidate. Furthermore, any regulatory approval to market a product may be subject to limitations on the indicated uses for which we may market the product. These limitations may limit the size of the market for the product and affect reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process includes all of the risks associated with FDA approval described above as well as risks attributable to the satisfaction of local regulations in foreign jurisdictions. Approval by the FDA does not assure approval by regulatory authorities outside the United States and vice versa.

If our pre-clinical testing does not produce successful results or our clinical trials do not demonstrate safety and efficacy in humans, we will not be able to commercialize our drug candidates.

Before obtaining regulatory approval for the sale of our drug candidates, we must conduct, at our own expense, extensive pre-clinical tests and clinical trials to demonstrate the safety and efficacy in humans of our drug candidates. Pre-clinical and clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and interim results of a clinical trial do not necessarily predict final results.

A failure of one of more of our clinical trials can occur at any stage of testing. We may experience numerous unforeseen events during, or as a result of, pre-clinical testing and the clinical trial process that could delay or prevent our ability to receive regulatory approval or commercialize our drug candidates, including:

regulators or IRBs may not authorize us to commence or continue a clinical trial or conduct a clinical trial at a prospective trial site;

our pre-clinical tests or clinical trials may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional pre-clinical testing or clinical trials, or we may abandon projects that we expect to be promising;

enrollment in our clinical trials may be slower than we anticipate or participants may drop out of our clinical trials at a higher rate than we anticipate, resulting in significant delays;

our third party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner;

we might have to suspend or terminate our clinical trials if the participants are being exposed to unacceptable health risks;

IRBs or regulators, including the FDA, may require that we hold, suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements;

the cost of our clinical trials may be greater than we anticipate;

the supply or quality of our drug candidates or other materials necessary to conduct our clinical trials may be insufficient or inadequate;

effects of our drug candidates may not be the desired effects or may include undesirable side effects or the drug candidates may have other unexpected characteristics; and

effects of our drug candidates may not be clear, or we may disagree with regulatory authorities, including the FDA, about how to interpret the data generated in our clinical trials.

Even if we obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory review. If we fail to comply with continuing United States and foreign regulations, we could lose our approvals to market drugs and our business would be seriously harmed.

Following any initial regulatory approval of any drugs we may develop, we will also be subject to continuing regulatory review, including the review of adverse drug experiences and clinical results that are reported after our drug products are made commercially available. This would include results from any post-marketing tests or vigilance required as a condition of approval. The manufacturer and manufacturing facilities we use to make any of our drug candidates will also be subject to periodic review and inspection by the FDA. The discovery of any new or previously unknown problems with the product, manufacturer or facility may result in restrictions on the drug or manufacturer or facility, including withdrawal of the drug from the market. We do not have, and currently do not intend to develop, the ability to manufacture material for our clinical trials or on a commercial scale. We may manufacture clinical trial materials or we may contract a third party to manufacture these materials for us. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the third-party manufacturer for regulatory compliance. Our product promotion and advertising is also subject to regulatory requirements and continuing regulatory review.

If we fail to comply with applicable continuing regulatory requirements, we may be subject to fines, suspension or withdrawal of regulatory approval, product recalls and seizures, operating restrictions and criminal prosecution.

Even if we receive regulatory approval to market our product candidates, the market may not be receptive to our product candidates upon their commercial introduction, which will prevent us from becoming profitable.

The product candidates that we are developing are based upon new technologies or therapeutic approaches. Key participants in pharmaceutical marketplaces, such as physicians, third-party payors and consumers, may not accept a product intended to improve therapeutic results based on RNAi technology. As a result, it may be more difficult for us to convince the medical community and third-party payors to accept and use our product, or to provide favorable reimbursement.

Other factors that we believe will materially affect market acceptance of our product candidates include:

- the timing of our receipt of any marketing approvals, the terms of any approvals and the countries in which approvals are obtained;
- the safety, efficacy and ease of administration of our product candidates;
- the willingness of patients to accept potentially new routes of administration;

the success of our physician education programs;

the availability of government and third-party payor reimbursement;

the pricing of our products, particularly as compared to alternative treatments; and

availability of alternative effective treatments for the diseases that product candidates we develop are intended to treat and the relative risks, benefits and costs of the treatments.

Even if we develop a RNAi therapeutic product for the prevention or treatment of infection by hemorrhagic fever viruses such as Ebola, governments may not elect to purchase such a product, which could adversely affect our business.

We expect that governments will be the only purchasers of any products we may develop for the prevention or treatment of hemorrhagic fever viruses such as Ebola. In the future, we may also initiate additional programs for the development of product candidates for which governments may be the only or primary purchasers. However, governments will not be required to purchase any such products from us and may elect not to do so, which could adversely affect our business. For example, although the focus of our Ebola program is to develop RNAi therapeutic targeting gene sequences that are highly conserved across known Ebola viruses, if the sequence of any Ebola virus that emerges is not sufficiently similar to those we are targeting, any product candidate that we develop may not be effective against that virus. Accordingly, while we expect that any RNAi therapeutic we develop for the treatment of Ebola could be stockpiled by governments as part of their biodefense preparations, they may not elect to purchase such product, or if they purchase our products, they may not do so at prices and volume levels that are profitable for us.

If we or our collaborators, manufacturers or service providers fail to comply with regulatory laws and regulations, we or they could be subject to enforcement actions, which could affect our ability to market and sell our products and may harm our reputation.

If we or our collaborators, manufacturers or service providers fail to comply with applicable federal, state or foreign laws or regulations, we could be subject to enforcement actions, which could affect our ability to develop, market and sell our products successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include:

warning letters;

product recalls or public notification or medical product safety alerts to healthcare professionals;

restrictions on, or prohibitions against, marketing our products;

restrictions on importation or exportation of our products;

suspension of review or refusal to approve pending applications;

exclusion from participation in government-funded healthcare programs;

exclusion from eligibility for the award of government contracts for our products;

suspension or withdrawal of product approvals;

product seizures;

injunctions; and

civil and criminal penalties and fines.

Any drugs we develop may become subject to unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives, thereby harming our business.

The regulations that govern marketing approvals, pricing and reimbursement for new drugs vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Although we intend to monitor these regulations, our programs are currently in the early stages of development and we will not be able to assess the impact of price regulations for a number of years. As a result, we might obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product and negatively impact the revenues we are able to generate from the sale of the product in that country.

Our ability to commercialize any products successfully also will depend in part on the extent to which reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Even if we succeed in bringing one or more products to the market, these products may not be considered cost-effective, and the amount reimbursed for any products may be insufficient to allow us to sell our products on a competitive basis. Because our programs are in the early stages of development, we are unable at this time to determine their cost effectiveness or the likely level or method of reimbursement. Increasingly, the third-party payors who reimburse patients, such as government and private insurance plans, are requiring that drug companies provide them with predetermined discounts from list prices, and are seeking to reduce the prices charged for pharmaceutical products. If the price we are able to charge for any products we develop is inadequate in light of our development and other costs, our profitability could be adversely affected.

We currently expect that any drugs we develop may need to be administered under the supervision of a physician. Under currently applicable United States law, drugs that are not usually self-administered may be eligible for coverage by the Medicare program if:

- they are incident to a physician s services;
- they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standard of medical practice;
- they are not excluded as immunizations; and
- they have been approved by the FDA.

There may be significant delays in obtaining coverage for newly-approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA. Moreover, eligibility for coverage does not imply that any drug will be reimbursed in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution. Interim payments for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement may be based on payments allowed for lower-cost drugs that are already reimbursed, may be incorporated into existing payments for other services and may reflect budgetary constraints or imperfections in Medicare data. Net prices for drugs may be reduced by mandatory discounts or rebates required by government health care programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Third party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for new drugs that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory proposals to change the healthcare system in the United States and other major healthcare markets have been proposed in recent years. These proposals have included prescription drug benefit legislation that was enacted and took effect in January 2006 and healthcare reform legislation recently enacted by certain states. Further federal and state legislative and regulatory developments are possible and we expect ongoing initiatives in the United States to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from drug candidates that we may successfully develop.

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Another development that may affect the pricing of drugs is Congressional action regarding drug reimportation into the United States. Recent proposed legislation has been introduced in Congress that, if enacted, would permit more widespread re-importation of drugs from foreign countries into the United States. This could include reh-importation from foreign countries where the drugs are sold at lower prices than in the United States. Such legislation, or similar regulatory changes, could lead to a decrease in the price we receive for any approved products, which, in turn, could impair our ability to generate revenue. Alternatively, in response to legislation such as this, we might elect not to seek approval for or market our products in foreign jurisdictions in order to minimize the risk of re-importation, which could also reduce the revenue we generate from our product sales.

There is a substantial risk of product liability claims in our business. If we are unable to obtain sufficient insurance, a product liability claim against us could adversely affect our business.

Our business exposes us to significant potential product liability risks that are inherent in the development, manufacturing and marketing of human therapeutic products. Product liability claims could delay or prevent completion of our clinical development programs. If we succeed in marketing products, such claims could result in an FDA investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs, and potentially a recall of our products or more serious enforcement action, limitations on the indications for which they may be used, or suspension or withdrawal of approvals. We currently have product liability insurance that we believe is appropriate for our stage of development and may need to obtain higher levels prior to marketing any of our drug candidates. Any insurance we have or may obtain may not provide sufficient coverage against potential liabilities. Furthermore, clinical trial and product liability insurance is becoming increasingly expensive. As a result, we may be unable to obtain sufficient insurance at a reasonable cost to protect us against losses caused by product liability claims that could have a material adverse effect on our business.

If we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research and development involves the use of hazardous materials, chemicals and various radioactive compounds. We maintain quantities of various flammable and toxic chemicals in our facilities in Cambridge that are required for our research and development activities. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. We believe our procedures for storing, handling and disposing these materials in our Cambridge facility comply with the relevant guidelines of the City of Cambridge and the Commonwealth of Massachusetts. Although we believe that our safety procedures for handling and disposing of these materials comply with the standards mandated by applicable regulations, the risk of accidental contamination or injury from these materials cannot be eliminated. If an accident occurs, we could be held liable for resulting damages, which could be substantial. We are also subject to numerous environmental, health and workplace safety laws and regulations, including those governing laboratory procedures, exposure to blood-borne pathogens and the handling of biohazardous materials.

Although we maintain workers   compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of these materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials. Additional federal, state and local laws and regulations affecting our operations may be adopted in the future. We may incur substantial costs to comply with, and substantial fines or penalties if we violate, any of these laws or regulations.

Risks Related to Patents, Licenses and Trade Secrets

If we are not able to obtain and enforce patent protection for our discoveries, our ability to develop and commercialize our product candidates will be harmed.

Our success depends, in part, on our ability to protect proprietary methods and technologies that we develop under the patent and other intellectual property laws of the United States and other countries, so that we can prevent others from unlawfully using our inventions and proprietary information. However, we may not hold proprietary rights to some patents required for us to commercialize our proposed products. Because certain U.S. patent applications are confidential until the patents issue, such as applications filed prior to November 29, 2000, or applications filed after such date which will not be filed in foreign countries, third parties may have filed patent applications for technology covered by our pending patent applications without our being aware of those applications, and our patent applications may not have priority over those applications. For this and other reasons, we may be unable to secure desired patent rights, thereby losing desired exclusivity. Further, we may be required to obtain licenses under third-party patents to market our proposed products or conduct our research and development or other activities. If licenses are not available to us on acceptable terms, we will not be able to market the affected products or conduct the desired activities.

Our strategy depends on our ability to rapidly identify and seek patent protection for our discoveries. In addition, we may rely on third-party collaborators to file patent applications relating to proprietary technology that we develop jointly during certain collaborations. The process of obtaining patent protection is expensive and time-consuming. If our present or future collaborators fail to file and prosecute all necessary and desirable patent applications at a reasonable cost and in a timely manner, our business will be adversely affected. Despite our efforts and the efforts of our collaborators to protect our proprietary rights, unauthorized parties may be able to obtain and use information that we regard as proprietary. While issued patents are presumed valid, this does not guarantee that the patent will survive a validity challenge or be held enforceable. Any patents we have obtained, or obtain in the future, may be challenged, invalidated, adjudged unenforceable or circumvented by parties attempting to design around our intellectual property. Moreover, third parties or the USPTO may commence interference proceedings involving our patents or patent applications. Any challenge to, finding of unenforceability or invalidation or circumvention of, our patents or patent applications would be costly, would require significant time and attention of our management and could have a material adverse effect on our business.

Our pending patent applications may not result in issued patents. The patent position of pharmaceutical or biotechnology companies, including ours, is generally uncertain and involves complex legal and factual considerations. The standards that the USPTO and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. Adding to the uncertainty of our current intellectual property portfolio and our ability to secure and enforce future patent rights are the outcome of a legal dispute surrounding the implementation of certain continuation and claims rules promulgated by the USPTO, which were scheduled to take effect November 1, 2007, but which are now enjoined and on appeal, and the outcome of Congressional efforts to reform the Patent Act of 1952. There is also no uniform, worldwide policy regarding the subject matter and scope of claims granted or allowable in pharmaceutical or biotechnology patents. Accordingly, we do not know the degree of future protection for our proprietary rights or the breadth of claims that will be allowed in any patents issued to us or to others.

We also rely to a certain extent on trade secrets, know-how and technology, which are not protected by patents, to maintain our competitive position. If any trade secret, know-how or other technology not protected by a patent were to be disclosed to or independently developed by a competitor, our business and financial condition could be materially adversely affected.

We license patent rights from third party owners. If such owners do not properly maintain or enforce the patents underlying such licenses, our competitive position and business prospects will be harmed.

We are a party to a number of licenses that give us rights to third party intellectual property that is necessary or useful for our business. In particular, we have obtained licenses from, among others, Isis, MIT, the Whitehead Institute for Biomedical Research, Max Planck Innovation, Stanford University, Tekmira and UTSW. We also intend to enter into additional licenses to third party intellectual property in the future.

Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, in particular, those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications to which we are licensed. Even if patents issue in respect of these patent applications, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue such litigation less aggressively than we would. Without protection for the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects.

Other companies or organizations may challenge our patent rights or may assert patent rights that prevent us from developing and commercializing our products.

RNA interference is a relatively new scientific field, the commercial exploitation of which has resulted in many different patents and patent applications from organizations and individuals seeking to obtain patent protection in the field. We have obtained grants and issuances of RNAi patents and have licensed many of these patents from third parties on an exclusive basis. The issued patents and pending patent applications in the United States and in key markets around the world that we own or license claim many different methods, compositions and processes relating to the discovery, development, manufacture and commercialization of RNAi therapeutics. Specifically, we have a portfolio of patents, patent applications and other intellectual property covering: fundamental aspects of the structure and uses of siRNAs, including their manufacture and use as therapeutics, and RNAi-related mechanisms; chemical modifications to siRNAs that improve their suitability for therapeutic uses; siRNAs directed to specific targets as treatments for particular diseases; and delivery technologies, such as in the field of cationic liposomes.

As the field of RNAi therapeutics is maturing, patent applications are being fully processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. It is likely that there will be significant litigation and other proceedings, such as interference, reexamination and opposition proceedings, in various patent offices relating to patent rights in the RNAi field. For example, various third parties have initiated oppositions to patents in our Kreutzer-Limmer and Tuschl II series in the EPO and in other jurisdictions. We expect that additional oppositions will be filed in the EPO and elsewhere, and other challenges will be raised relating to other patents and patent applications in our portfolio. In many cases, the possibility of appeal exists for either us or our opponents, and it may be years before final, unappealable rulings are made with respect to these patents in certain jurisdictions. The timing and outcome of these and other proceedings is uncertain and may adversely affect our business if we are not successful in defending the patentability and scope of our pending and issued patent claims. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material adverse effect on our business and our ability to successfully compete in the field of RNAi.

There are many issued and pending patents that claim aspects of oligonucleotide chemistry that we may need to apply to our siRNA drug candidates. There are also many issued patents that claim targeting genes or portions of genes that may be relevant for siRNA drugs we wish to develop. Thus, it is possible that one or more organizations will hold patent rights to which we will need a license. If those organizations refuse to grant us a license to such patent rights on reasonable terms, we may not be able to market products or perform research and development or other activities covered by these patents.

If we become involved in patent litigation or other proceedings related to a determination of rights, we could incur substantial costs and expenses, substantial liability for damages or be required to stop our product development and commercialization efforts.

Third parties may sue us for infringing their patent rights. Likewise, we may need to resort to litigation to enforce a patent issued or licensed to us or to determine the scope and validity of proprietary rights of others. In addition, a third party may claim that we have improperly obtained or used its confidential or proprietary information. Furthermore, in connection with a license agreement, we have agreed to indemnify the licensor for costs incurred in connection with litigation relating to intellectual property rights. The cost to us of any litigation or other proceeding relating to intellectual property rights, even if resolved in our favor, could be substantial, and the litigation would divert our management s efforts. Some of our competitors may be able to sustain the costs of complex patent litigation more effectively than we can because they have substantially greater resources. Uncertainties resulting from the initiation and continuation of any litigation could limit our ability to continue our operations.

If any parties successfully claim that our creation or use of proprietary technologies infringes upon their intellectual property rights, we might be forced to pay damages, potentially including treble damages, if we are found to have willfully infringed on such parties patent rights. In addition to any damages we might have to pay, a court could require us to stop the infringing activity or obtain a license. Any license required under any patent may not be made available on commercially acceptable terms, if at all. In addition, such licenses are likely to be non-exclusive and, therefore, our competitors may have access to the same technology licensed to us. If we fail to obtain a required license and are unable to design around a patent, we may be unable to effectively market some of our technology and products, which could limit our ability to generate revenues or achieve profitability and possibly prevent us from generating revenue sufficient to sustain our operations. Moreover, we expect that a number of our collaborations will provide that royalties payable to us for licenses to our intellectual property may be offset by amounts paid by our collaborators to third parties who have competing or superior intellectual property positions in the relevant fields, which could result in significant reductions in our revenues from products developed through collaborations.

If we fail to comply with our obligations under any licenses or related agreements, we could lose license rights that are necessary for developing and protecting our RNAi technology and any related product candidates that we develop, or we could lose certain exclusive rights to grant sublicenses.

Our current licenses impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, royalty, diligence, sublicensing, insurance and other obligations on us. If we breach any of these obligations, the licensor may have the right to terminate the license or render the license non-exclusive, which could result in us being unable to develop, manufacture and sell products that are covered by the licensed technology or enable a competitor to gain access to the licensed technology. In addition, while we cannot currently determine the amount of the royalty obligations we will be required to pay on sales of future products, if any, the amounts may be significant. The amount of our future royalty obligations will depend on the technology and intellectual property we use in products that we successfully develop and commercialize, if any. Therefore, even if we successfully develop and commercialize products, we may be unable to achieve or maintain profitability.

Confidentiality agreements with employees and others may not adequately prevent disclosure of trade secrets and other proprietary information.

In order to protect our proprietary technology and processes, we rely in part on confidentiality agreements with our collaborators, employees, consultants, outside scientific collaborators and sponsored researchers and other advisors. These agreements may not effectively prevent disclosure of confidential information and may not provide an adequate remedy in the event of unauthorized disclosure of confidential information. In addition, others may independently discover trade secrets and proprietary information, and in such cases we could not assert any trade secret rights against such party. Costly and time-consuming litigation could be necessary to enforce and determine the scope of our proprietary rights, and failure to obtain or maintain trade secret protection could adversely affect our competitive business position.

Risks Related to Competition

The pharmaceutical market is intensely competitive. If we are unable to compete effectively with existing drugs, new treatment methods and new technologies, we may be unable to commercialize successfully any drugs that we develop.

The pharmaceutical market is intensely competitive and rapidly changing. Many large pharmaceutical and biotechnology companies, academic institutions, governmental agencies and other public and private research organizations are pursuing the development of novel drugs for the same diseases that we are targeting or expect to target. Many of our competitors have:

much greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products;

more extensive experience in pre-clinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing, marketing and selling pharmaceutical products;

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product candidates that are based on previously tested or accepted technologies;

products that have been approved or are in late stages of development; and

collaborative arrangements in our target markets with leading companies and research institutions.

We will face intense competition from drugs that have already been approved and accepted by the medical community for the treatment of the conditions for which we may develop drugs. We also expect to face competition from new drugs that enter the market. We believe a significant number of drugs are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop drugs. For instance, we are currently evaluating RNAi therapeutics for RSV, liver cancer, hypercholesterolemia, TTR amyloidosis and HD, and have a number of additional discovery programs targeting other diseases. Virazole and Synagis are currently marketed for the treatment of certain RSV patients, and numerous drugs are currently marketed or used for the treatment of liver cancer, hypercholesterolemia and HD as well. These drugs, or other of our competitors products, may be more effective, safer, less expensive or marketed and sold more effectively, than any products we develop.

If we successfully develop drug candidates, and obtain approval for them, we will face competition based on many different factors, including:

the safety and effectiveness of our products;

the ease with which our products can be administered and the extent to which patients accept relatively new routes of administration;

the timing and scope of regulatory approvals for these products;

the availability and cost of manufacturing, marketing and sales capabilities;

price;

reimbursement coverage; and

patent position.

Our competitors may develop or commercialize products with significant advantages over any products we develop based on any of the factors listed above or on other factors. Our competitors may therefore be more successful in commercializing their products than we are, which could adversely affect our competitive position and business. Competitive products may make any products we develop obsolete or noncompetitive before we can recover the expenses of developing and commercializing our drug candidates. Furthermore, we also face competition from existing and new treatment methods that reduce or eliminate the need for drugs, such as the use of advanced medical devices. The development of new medical devices or other treatment methods for the diseases we are targeting could make our drug candidates noncompetitive, obsolete or uneconomical.

We face competition from other companies that are working to develop novel drugs using technology similar to ours. If these companies develop drugs more rapidly than we do or their technologies, including delivery technologies, are more effective, our ability to successfully commercialize drugs will be adversely affected.

In addition to the competition we face from competing drugs in general, we also face competition from other companies working to develop novel drugs using technology that competes more directly with our own. We are aware of several companies that are working in the field of RNAi. In addition, we granted licenses or options for licenses to Isis, GeneCare, Benitec, Calando, Tekmira, Quark and others under which these companies may independently develop RNAi therapeutics against a limited number of targets. Any of these companies may develop its RNAi technology more rapidly and more effectively than us. Merck was one of our collaborators and a licensee under our intellectual property for specified disease targets until September 2007, at which time we and Merck agreed to terminate our collaboration. As a result of its acquisition of Sirna Therapeutics Inc. in December 2006, and in light of the mutual termination of our collaboration, Merck, which has substantially more resources and experience in developing drugs than we do, may become a direct competitor.

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In addition, as a result of agreements that we have entered into, Roche and Takeda have obtained, and Novartis has the right to obtain, broad, non-exclusive licenses to certain aspects of our technology that give them the right to compete with us in certain circumstances.

We also compete with companies working to develop antisense-based drugs. Like RNAi product candidates, antisense drugs target messenger RNAs, or mRNAs, in order to suppress the activity of specific genes. Isis is currently marketing an antisense drug and has several antisense drug candidates in clinical trials. The development of antisense drugs is more advanced than that of RNAi therapeutics, and antisense technology may become the preferred technology for drugs that target mRNAs to silence specific genes.

In addition to competition with respect to RNAi and with respect to specific products, we face substantial competition to discover and develop safe and effective means to deliver siRNAs to the relevant cell and tissue types. Safe and effective means to deliver siRNAs to the relevant cell and tissue types may be developed by our competitors, and our ability to successfully commercialize a competitive product would be adversely affected. In addition, substantial resources are being expended by third parties in the effort to discover and develop a safe and effective means of delivering siRNAs into the relevant cell and tissue types, both in academic laboratories and in the corporate sector. Some of our competitors have substantially greater resources than we do, and if our competitors are able to negotiate exclusive access to those delivery solutions developed by third parties, we may be unable to successfully commercialize our product candidates.

Risks Related to Our Common Stock

If our stock price fluctuates, purchasers of our common stock could incur substantial losses.

The market price of our common stock may fluctuate significantly in response to factors that are beyond our control. The stock market in general has recently experienced extreme price and volume fluctuations. The market prices of securities of pharmaceutical and biotechnology companies have been extremely volatile, and have experienced fluctuations that often have been unrelated or disproportionate to the operating performance of these companies. These broad market fluctuations could result in extreme fluctuations in the price of our common stock, which could cause purchasers of our common stock to incur substantial losses.

We may incur significant costs from class action litigation due to our expected stock volatility.

Our stock price may fluctuate for many reasons, including as a result of public announcements regarding the progress of our development efforts, the addition or departure of our key personnel, variations in our quarterly operating results and changes in market valuations of pharmaceutical and biotechnology companies. Recently, when the market price of a stock has been volatile as our stock price may be, holders of that stock have occasionally brought securities class action litigation against the company that issued the stock. If any of our stockholders were to bring a lawsuit of this type against us, even if the lawsuit is without merit, we could incur substantial costs defending the lawsuit. The lawsuit could also divert the time and attention of our management.

Novartis ownership of our common stock could delay or prevent a change in corporate control or cause a decline in our common stock should Novartis decide to sell all or a portion of its shares.

As of December 31, 2008, Novartis holds 13.2% of our outstanding common stock and has the right to maintain its ownership percentage through the expiration or termination of our broad alliance. This concentration of ownership may harm the market price of our common stock by:

- delaying, deferring or preventing a change in control of our company;

- impeding a merger, consolidation, takeover or other business combination involving our company; or
- discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of our company.

In addition, if Novartis decides to sell all or a portion of its shares in a rapid or disorderly manner, our stock price could be negatively impacted.

Anti-takeover provisions in our charter documents and under Delaware law and our stockholder rights plan could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws may delay or prevent an acquisition of us or a change in our management. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. These provisions include:

- a classified board of directors;
- a prohibition on actions by our stockholders by written consent;
- limitations on the removal of directors; and
- advance notice requirements for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings.

In addition our board of directors has adopted a stockholder rights plan, the provisions of which could make it difficult for a potential acquirer of Alnylam to consummate an acquisition transaction.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions would apply even if the proposed merger or acquisition could be considered beneficial by some stockholders.

ITEM 1B. UNRESOLVED STAFF COMMENTS.

Not applicable.

ITEM 2. PROPERTIES

Our operations are based primarily in Cambridge, Massachusetts. As of January 31, 2009, we lease approximately 84,000 square feet of office and laboratory space in Cambridge, Massachusetts. The two leases for this property expire in September 2011. We believe that the total space available to us under our current leases will meet our needs for the foreseeable future and that additional space would be available to us on commercially reasonable terms if required.

ITEM 3. LEGAL PROCEEDINGS

We are currently not a party to any material legal proceedings.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

No matters were submitted to a vote of our security holders during the fourth quarter of the fiscal year ended December 31, 2008.

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PART II

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

Market Information

Our common stock began trading on The NASDAQ Global Market on May 28, 2004 under the symbol ALNY . Prior to that time, there was no established public trading market for our common stock. The following table sets forth the high and low sale prices per share for our common stock on The NASDAQ Global Market for the periods indicated:

Year Ended December 31, 2007:	**High**	**Low**
First Quarter	$ 22.94	$16.66
Second Quarter	$ 20.68	$15.06
Third Quarter	$ 34.85	$14.87
Fourth Quarter	$ 37.35	$26.84

Year Ended December 31, 2008:	**High**	**Low**
First Quarter	$ 35.19	$ 22.25
Second Quarter	$ 30.74	$ 22.55
Third Quarter	$ 36.37	$ 25.07
Fourth Quarter	$ 28.95	$ 16.37

Holders of record

As of January 31, 2009, there were approximately 97 holders of record of our common stock. Because many of our shares are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of individual stockholders represented by these record holders.

Dividends

We have never paid or declared any cash dividends on our common stock. We currently intend to retain any earnings for future growth and, therefore, do not expect to pay cash dividends in the foreseeable future.

Securities Authorized for Issuance Under Equity Compensation Plans

Information relating to our equity compensation plans will be included in our proxy statement in connection with our 2009 Annual Meeting of Stockholders, under the caption Equity Compensation Plan Information. That portion of our proxy statement is incorporated herein by reference.

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Stock Performance Graph

The following performance graph and related information shall not be deemed soliciting material or to be filed with the SEC, nor shall such information be incorporated by reference into any future filing under the Securities Act of 1933 or Securities Exchange Act of 1934, each as amended, except to the extent that we specifically incorporate it by reference into such filing.

The comparative stock performance graph below compares the cumulative total stockholder return (assuming reinvestment of dividends, if any) from investing $100 on May 28, 2004, the date on which our common stock was first publicly traded, to the close of the last trading day of 2008, in each of (i) our common stock, (ii) the NASDAQ Stock Market (U.S.) Index and (iii) the NASDAQ Pharmaceutical Index.

Comparison of Cumulative Total Return
Among Alnylam Pharmaceuticals, Inc.,
NASDAQ Stock Market (U.S.) Index and NASDAQ Pharmaceuticals Index

	5/28/2004	12/31/2004	12/30/2005	12/29/2006	12/31/2007	12/31/2008
Alnylam Pharmaceuticals, Inc.	$ 100.00	$ 124.29	$ 222.30	$ 356.07	$ 483.86	$ 411.48
Nasdaq Stock Market (U.S.) Index	$ 100.00	$ 109.70	$ 112.03	$ 123.08	$ 133.48	$ 64.38
Nasdaq Pharmaceutical Index	$ 100.00	$ 103.32	$ 113.77	$ 111.36	$ 117.11	$ 108.98

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ITEM 6. SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data for each of the five years in the period ended December 31, 2008 are derived from our audited consolidated financial statements. The selected consolidated financial data set forth below should be read in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations and the financial statements, and the related Notes, included elsewhere in this annual report on Form 10-K. Historical results are not necessarily indicative of future results.

Selected Consolidated Financial Data
(In thousands, except per share data)

	Year Ended December 31,				
	2008	**2007**	**2006**	**2005**	**2004**
Statement of Operations Data:					
Net revenues	$ 96,163	$ 50,897	$ 26,930	$ 5,716	$ 4,278
Operating expenses(1)	123,998	144,074	66,431	49,188	36,542
Loss from operations	(27,835)	(93,177)	(39,501)	(43,472)	(32,264)
Net loss	(26,249)	(85,466)	(34,608)	(42,914)	(32,654)
Net loss attributable to common stockholders	$ (26,249)	$ (85,466)	$ (34,608)	$ (42,914)	$ (35,367)
Net loss per common share basic and diluted	$ (0.64)	$ (2.21)	$ (1.09)	$ (1.96)	$ (2.98)
Weighted average common shares outstanding basic and diluted	41,077	38,657	31,890	21,949	11,886
(1) Non-cash stock-based compensation included in operating expenses	$ 16,382	$ 14,472	$ 8,304	$ 4,597	$ 4,106

	December 31,				
	2008	**2007**	**2006**	**2005**	**2004**
Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 512,709	$ 455,602	$ 217,260	$ 80,002	$ 46,046
Working capital	342,797	314,427	199,859	63,930	41,606
Total assets	554,676	493,791	240,006	98,348	66,107
Notes payable		6,758	9,136	7,395	7,201
Total stockholders equity	202,125	199,168	201,174	61,779	46,142

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

Overview

We are a biopharmaceutical company developing novel therapeutics based on RNA interference, or RNAi. RNAi is a naturally occurring biological pathway within cells for selectively silencing and regulating the expression of specific genes. Since many diseases are caused by the inappropriate activity of specific genes, the ability to silence genes selectively through RNAi could provide a new way to treat a wide range of human diseases. We believe that drugs that work through RNAi have the potential to become a broad new class of drugs, like small molecule, protein and antibody drugs. Using our intellectual property and the expertise we have built in RNAi, we are developing a set of biological and chemical methods and know-how that we apply in a systematic way to develop RNAi therapeutics for a variety of diseases.

We are applying our technological expertise to build a pipeline of RNAi therapeutics to address significant medical needs, many of which cannot effectively be addressed with small molecules or antibodies, the current major classes of drugs. Our lead RNAi therapeutic program, ALN-RSV01, is in Phase II clinical trials for the treatment of human respiratory syncytial virus, or RSV, infection, which is reported to be the leading cause of hospitalization in infants in the United States and also occurs in the elderly and in immune compromised adults. In February 2008, we reported positive results from our Phase II experimental RSV infection clinical trial, referred to as the GEMINI study. In April 2008, we initiated a second Phase II human clinical trial, which is currently ongoing, to assess the safety and tolerability of aerosolized ALN-RSV01 versus placebo in adult lung transplant patients naturally infected with RSV. We recently formed collaborations with Cubist Pharmaceuticals, Inc., or Cubist, and Kyowa Hakko Kirin Co., Ltd., or Kyowa Hakko, for the development and commercialization of products for RSV. We will jointly develop and commercialize products for RSV in partnership with Cubist in North America, Cubist has responsibility for developing and commercializing these products in the rest of the world outside of Asia, and Kyowa Hakko has the responsibility for developing and commercializing these products in Asia.

In December 2008, we submitted an investigational new drug application, or IND, to the United States Food and Drug Administration, or FDA, for ALN-VSP, our first systemically delivered RNAi therapeutic candidate. We are developing ALN-VSP for the treatment of liver cancers, including hepatocellular carcinoma and other solid tumors with liver involvement. We received clearance from the FDA in January 2009 to proceed with a Phase I study. We expect to initiate this study during the first half of 2009. The Phase I study will be a multi-center, open label, dose escalation trial to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of intravenous ALN-VSP in patients with advanced solid tumors with liver involvement.

We are also working on a number of programs in pre-clinical development, including:

- ALN-PCS, an RNAi therapeutic candidate targeting a gene called proprotein convertase subtilisin/kexin type 9, or PCSK9, for the treatment of hypercholesterolemia;

- ALN-TTR, an RNAi therapeutic candidate targeting the transthyretin, or TTR, gene, for the treatment of TTR amyloidosis; and

- ALN-HTT, an RNAi therapeutic candidate targeting the huntingtin gene, for the treatment of Huntington s disease, which we are developing in collaboration with Medtronic, Inc., or Medtronic.

We have additional discovery programs for RNAi therapeutics for the treatment of a broad range of diseases.

In addition, we are working internally and with third-party collaborators to develop capabilities to deliver our RNAi therapeutics directly to specific sites of disease, such as the delivery of ALN-RSV01 to the lungs, which we refer to as Direct RNAi. We are also working to extend our capabilities to advance the development of RNAi therapeutics that are administered by intravenous, subcutaneous or intramuscular approaches, which we refer to as Systemic RNAi. We have numerous RNAi therapeutic delivery collaborations and intend to continue to collaborate with government, academic and corporate third parties to evaluate different delivery options, including with respect to Direct RNAi and Systemic RNAi.

We rely on the strength of our intellectual property portfolio relating to the development and commercialization of small interfering RNAs, or siRNAs, as therapeutics. This includes ownership of, or exclusive rights to, issued patents and pending patent applications claiming fundamental features of siRNAs and RNAi therapeutics as well as those claiming crucial chemical modifications and promising delivery technologies. We believe that no other company possesses a portfolio of such broad and exclusive rights to the patents and patent applications required for the commercialization of RNAi therapeutics. Given the importance of our intellectual property portfolio to our business operations, we intend to vigorously enforce our rights and defend against any challenges that have arisen or may arise in this area.

In addition, our expertise in RNAi therapeutics and broad intellectual property estate have allowed us to form alliances with leading companies, including Isis Pharmaceuticals, Inc., or Isis, Medtronic, Novartis Pharma AG, or Novartis, Biogen Idec Inc., or Biogen Idec, F. Hoffmann-La Roche Ltd, or Roche, Takeda Pharmaceutical Company Limited, or Takeda, Kyowa Hakko and Cubist. We have also entered into contracts with government agencies, including the National Institute of Allergy and Infectious Diseases, or NIAID, a component of the National Institutes of Health, or NIH. We have established collaborations with and, in some instances, received funding from major medical and disease associations. Finally, to further enable the field and monetize our intellectual property rights, we also grant licenses to biotechnology companies for the development and commercialization of RNAi therapeutics for specified targets in which we have no direct strategic interest under our InterfeRx™ program and to research companies that commercialize RNAi reagents or services under our research product licenses.

We also seek opportunities to form new ventures in areas outside our core strategic interest. For example, in 2007, we and Isis established Regulus Therapeutics LLC, or Regulus Therapeutics, a company focused on the discovery, development and commercialization of microRNA-based therapeutics. Because microRNAs are believed to regulate whole networks of genes that can be involved in discrete disease processes, microRNA-based therapeutics represent a possible new approach to target the pathways of human disease. Given the broad applications for RNAi technology, we believe additional opportunities exist for new ventures to be formed.

Alnylam commenced operations in June 2002. We have focused our efforts since inception primarily on business planning, research and development, acquiring, filing and expanding intellectual property rights, recruiting management and technical staff, and raising capital. Since our inception, we have generated significant losses. As of December 31, 2008, we had an accumulated deficit of $252.2 million. Through December 31, 2008, we have funded our operations primarily through the net proceeds from the sale of equity securities and payments we have received under strategic alliances. Through December 31, 2008, a substantial portion of our total net revenues have been collaboration revenues derived from our strategic alliances with Roche, Takeda and Novartis, and from the United States government in connection with our development of treatments for hemorrhagic fever viruses, including Ebola. We expect our revenues to continue to be derived primarily from new and existing strategic alliances, government and foundation funding and license fee revenues.

We currently have programs focused in a number of therapeutic areas. However, we are unable to predict when, if ever, we will successfully develop or be able to commence sales of any product. We have never achieved profitability on an annual basis and we expect to incur additional losses over the next several years. We expect our net losses to continue due primarily to research and development activities relating to our drug development programs, collaborations and other general corporate activities. We anticipate that our operating results will fluctuate for the foreseeable future. Therefore, period-to-period comparisons should not be relied upon as predictive of the results in future periods. Our sources of potential funding for the next several years are expected to be derived primarily from payments under new and existing strategic alliances, which may include license and other fees, funded research and development payments and milestone payments, government and foundation funding and proceeds from the sale of equity.

Research and Development

Since our inception, we have focused on drug discovery and development programs. Research and development expenses represent a substantial percentage of our total operating expenses. Our most advanced program is focused on the treatment of RSV infection and is in Phase II clinical studies. In January 2009, we received clearance from the FDA to proceed with a Phase I study of ALN-VSP for the treatment of liver cancers and potentially other solid tumors. Our other development programs are focused on the treatment of hypercholesterolemia, TTR amyloidosis and Huntington s disease. We also have discovery programs to develop RNAi therapeutics for the treatment of a broad range of diseases, such as viral hemorrhagic fever, including the Ebola virus, progressive multifocal leukoencephalopathy, or PML, Parkinson s disease and many other undisclosed programs, as well as several other diseases that are the subject of our strategic alliances. In addition, we are working internally and with third-party collaborators to develop capabilities to deliver our RNAi therapeutics both directly to the specific sites of disease and systemically, and we intend to continue to collaborate with government, academic and corporate third parties to evaluate different delivery options.

There is a risk that any drug discovery or development program may not produce revenue for a variety of reasons, including the possibility that we will not be able to adequately demonstrate the safety and efficacy of the product candidate. Moreover, there are uncertainties specific to any new field of drug discovery, including RNAi. The successful development of any product candidate we develop is highly uncertain. Due to the numerous risks associated with developing drugs, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts necessary to complete the development of, or the period, if any, in which material net cash inflows will commence from, any potential product candidate. These risks include the uncertainty of:

- our ability to progress product candidates into pre-clinical and clinical trials;
- the scope, rate and progress of our pre-clinical trials and other research and development activities, including those related to developing safe and effective ways of delivering siRNAs into cells and tissues;
- the scope, rate of progress and cost of any clinical trials we commence;
- clinical trial results;
- the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the terms, timing and success of any collaborative, licensing and other arrangements that we may establish;
- the cost, timing and success of regulatory filings and approvals;
- the cost and timing of establishing sufficient sales, marketing and distribution capabilities;
- the cost and timing of establishing sufficient clinical and commercial supplies of any products that we may develop; and
- the effect of competing technological and market developments.

Any failure to complete any stage of the development of any potential products in a timely manner could have a material adverse effect on our operations, financial position and liquidity. A discussion of some of the risks and uncertainties associated with completing our projects on schedule, or at all, and the potential consequences of failing to do so, are set forth in Item 1A above under the heading Risk Factors.

Strategic Alliances

A significant component of our business plan is to enter into strategic alliances and collaborations with pharmaceutical and biotechnology companies, academic institutions, research foundations and others, as appropriate, to gain access to funding, capabilities, technical resources and intellectual property to further our development efforts and to generate revenues. Our collaboration strategy is to form (1) non-exclusive platform alliances where our collaborators obtain access to our capabilities and intellectual property to develop their own RNAi therapeutic products; and (2) 50-50 co-development and/or ex-U.S. market geographic partnerships on specific RNAi therapeutic programs. We have entered into broad, non-exclusive platform license agreements with Roche and Takeda, under which we will also collaborate with each of Roche and Takeda on RNAi drug discovery for one or more disease targets. We are pursuing 50-50 co-development programs with Cubist and Medtronic for the development and commercialization of ALN-RSV and ALN-HTT, respectively. In addition, we have entered into a product alliance with Kyowa Hakko for the development and commercialization of ALN-RSV in territories not covered by the Cubist agreement, which include Japan and other markets in Asia. We also have discovery and development alliances with Isis, Novartis and Biogen Idec.

We also seek opportunities to form new ventures in areas outside our core strategic interest. For example, we formed Regulus Therapeutics, together with Isis, to capitalize on our technology and intellectual property in the field of microRNA-based therapeutics. Given the broad applications for RNAi technology, we believe additional opportunities exist for new ventures to be formed.

To generate revenues from our intellectual property rights, we also grant licenses to biotechnology companies under our InterfeRx program for the development and commercialization of RNAi therapeutics for specified targets in which we have no direct strategic interest. We also license key aspects of our intellectual property to companies active in the research products and services market, which includes the manufacture and sale of reagents. Our InterfeRx and research product licenses aim to generate modest near-term revenues that we can re-invest in the development of our proprietary RNAi therapeutics pipeline. As of January 31, 2009, we had granted such licenses, on both an exclusive and nonexclusive basis, to approximately 20 companies.

Since delivery of RNAi therapeutics remains a major objective of our research activities, we also look to form collaboration and licensing agreements with other companies and academic institutions to gain access to delivery technologies. For example, we have formed agreements with Tekmira Pharmaceuticals Corporation, or Tekmira, and Massachusetts Institute of Technology, or MIT, among others, to focus on various delivery strategies. We have also entered into license agreements with Isis, Max Planck Innovation, Tekmira and MIT, as well as a number of other entities, to obtain rights to important intellectual property in the field of RNAi.

Finally, we seek funding for the development of our proprietary RNAi therapeutics pipeline from foundations and government sources. In 2006, NIAID awarded us a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus. In 2007, the Defense Threat Reduction Agency, or DTRA, an agency of the United States Department of Defense, awarded us a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus, which contract ended in February 2009. In addition, we have obtained funding for pre-clinical discovery programs from organizations such as The Michael J. Fox Foundation.

In September 2007, we terminated our amended and restated research collaboration and license agreement with Merck & Co., Inc., or Merck. Pursuant to the termination agreement, all license grants of intellectual property to develop, manufacture and/or commercialize RNAi therapeutic products under the amended and restated research collaboration and license agreement ceased as of the date of the termination agreement, subject to certain specified exceptions. The termination agreement further provides that, subject to certain conditions, we and Merck will each retain sole ownership and rights in our own intellectual property.

Platform Alliances.

Roche. In July 2007, we and, for limited purposes, Alnylam Europe AG, or Alnylam Europe, entered into a license and collaboration agreement with Roche. Under the license and collaboration agreement, which became effective in August 2007, we granted Roche a non-exclusive license to our intellectual property to develop and commercialize therapeutic products that function through RNAi, subject to our existing contractual obligations to third parties. The license is initially limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases, and may be expanded to include up to 18 additional therapeutic areas, comprising all other fields of human disease, as identified and agreed upon by the parties, upon payment to us by Roche of an additional $50.0 million for each additional therapeutic area, if any.

In consideration for the rights granted to Roche under the license and collaboration agreement, Roche paid us $273.5 million in upfront cash payments. In addition, in exchange for our contributions under the collaboration agreement, for each RNAi therapeutic product successfully developed by Roche, its affiliates or sublicensees under the collaboration agreement, if any, we are entitled to receive milestone payments upon achievement of specified development and sales events, totaling up to an aggregate of $100.0 million per therapeutic target, together with royalty payments based on worldwide annual net sales, if any. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any milestone or royalty payments from Roche.

Under the license and collaboration agreement, we and Roche also agreed to collaborate on the discovery of RNAi therapeutic products directed to one or more disease targets, subject to our contractual obligations to third parties. The discovery collaboration between Roche and us will be governed by a joint steering committee for a period of five years that is comprised of an equal number of representatives from each party. In exchange for our contributions to the collaboration, Roche will be required to make additional milestone and royalty payments to us.

In connection with the execution of the license and collaboration agreement, we executed a common stock purchase agreement with Roche Finance Ltd, or Roche Finance, an affiliate of Roche. Under the terms of the common stock purchase agreement, in August 2007, Roche Finance purchased 1,975,000 shares of our common stock at $21.50 per share, for an aggregate purchase price of $42.5 million.

In connection with the execution of the license and collaboration agreement and the common stock purchase agreement, we also executed a stock purchase agreement with Alnylam Europe and Roche Beteiligungs GmbH, or Roche Germany, an affiliate of Roche. Under the terms of the Alnylam Europe stock purchase agreement, we created a new, wholly-owned German limited liability company, Roche Kulmbach, into which substantially all of the non-intellectual property assets of Alnylam Europe were transferred, and Roche Germany purchased from us all of the issued and outstanding shares of Roche Kulmbach for an aggregate purchase price of $15.0 million. The Alnylam Europe stock purchase agreement included transition services that were performed by Roche Kulmbach employees at various levels through August 2008. We reimbursed Roche for these services at an agreed-upon rate.

In connection with the license and collaboration agreement and the common stock purchase agreement, we paid $27.5 million in license fees to our licensors, primarily Isis, in accordance with the applicable license agreements with those parties.

Takeda. In May 2008, we entered into a license and collaboration agreement with Takeda to pursue the development and commercialization of RNAi therapeutics. Under the Takeda agreement, we granted to Takeda a non-exclusive, worldwide, royalty-bearing license to our intellectual property to develop, manufacture, use and commercialize RNAi therapeutics, subject to our existing contractual obligations to third parties. The license initially is limited to the fields of oncology and metabolic disease and may be expanded at Takeda s option to include other therapeutic areas, subject to specified conditions. Under the Takeda agreement, Takeda will be our exclusive platform partner in the Asian territory, as defined in the agreement, for a period of five years.

In consideration for the rights granted to Takeda under the Takeda agreement, Takeda agreed to pay us $150.0 million in upfront and near-term technology transfer payments. In addition, we have the option, exercisable until the start of Phase III development, to opt-in under a 50-50 profit sharing agreement to the development and commercialization in the United States of up to four Takeda licensed products, and would be entitled to opt-in rights for two additional products for each additional field expansion, if any, elected by Takeda under the Takeda agreement. In June 2008, Takeda paid us an upfront payment of $100.0 million. Takeda is also required to make the additional $50.0 million in payments to us upon achievement of specified technology transfer milestones, $20.0 million of which was achieved in September 2008 and paid in October 2008, $20.0 million of which is required to be paid within 12 to 24 months of execution of the agreement and $10.0 million of which is required to be paid within 24 to 36 months of execution of the agreement. If Takeda elects to expand its license to additional therapeutic areas, Takeda will be required to pay us $50.0 million for each of up to approximately 20 total additional fields selected, comprising all other fields of human disease, as identified and agreed upon by the parties. In addition, for each RNAi therapeutic product successfully developed by Takeda, its affiliates and sublicensees, if any, we are entitled to receive specified development and commercialization milestones, totaling up to $171.0 million per product, together with royalty payments based on worldwide annual net sales, if any. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any milestone or royalty payments from Takeda.

Pursuant to the Takeda agreement, we and Takeda have also agreed to collaborate on the research of RNAi therapeutics directed to one or two disease targets agreed to by the parties, subject to our existing contractual obligations with third parties. Takeda also has the option, subject to certain conditions, to collaborate with us on the research and development of RNAi drug delivery technology for targets agreed to by the parties. In addition, Takeda has a right of first negotiation for the development and commercialization of our RNAi therapeutic products in the Asian territory, excluding our ALN-RSV01 program. In addition to our 50-50 profit sharing option, we have a similar right of first negotiation to participate with Takeda in the development and commercialization in the United States of licensed products. The collaboration is governed by a joint technology transfer committee, or JTTC, a joint research collaboration committee, or JRCC, and a joint delivery collaboration committee, or JDCC, each of which is comprised of an equal number of representatives from each party.

In connection with the Takeda agreement, we paid $5.0 million of license fees to our licensors, primarily Isis, in accordance with the applicable license agreements with those parties.

Discovery and Development Alliances.

Isis. In March 2004, we entered into a collaboration and license agreement with Isis, a leading developer of antisense oligonucleotide drugs that target RNA. The Isis agreement significantly enhanced our intellectual property position with respect to RNA-based therapeutic products and our ability to develop siRNAs for RNAi therapeutic products, and provided us with the opportunity to defer investment in manufacturing technology. Isis granted us licenses to its current and future patents and patent applications relating to chemistry and to RNA-targeting mechanisms for the research, development and commercialization of siRNA products. We have the right to use Isis technologies in our development programs or in collaborations, and Isis has agreed not to grant licenses under these patents to any other organization for any siRNA products designed to work through an RNAi mechanism, except in the context of a collaboration in which Isis plays an active role. The licenses that we have granted to Isis are non-exclusive licenses to our current and future patents and patent applications relating to RNA-targeting mechanisms and to chemistry for research use. We have also granted Isis the non-exclusive right to develop and commercialize siRNA products against a limited number of targets. In addition, we have granted Isis non-exclusive rights to our patents and patent applications for research, development and commercialization of antisense RNA products.

Under the terms of the Isis agreement, we paid Isis an upfront license fee of $5.0 million. We also agreed to pay Isis milestone payments, totaling up to approximately $3.4 million, upon the occurrence of specified development and regulatory events, and royalties on sales, if any, for each product that we or a collaborator develops using Isis intellectual property. In addition, we agreed to pay to Isis a percentage of specified fees from strategic collaborations we may enter into that include access to the Isis intellectual property.

In conjunction with the agreement, Isis made a $10.0 million equity investment in us. In addition, Isis has agreed to pay us, per therapeutic target, a license fee of $0.5 million, and milestone payments totaling approximately $3.4 million, payable upon the occurrence of specified development and regulatory events, and royalties on sales, if any, for each product developed by Isis or a collaborator that utilizes our intellectual property. Isis has the right to elect up to ten non-exclusive target licenses under the agreement and has the right to purchase one additional non-exclusive target per year during the term of the collaboration.

The Isis agreement also gives us an option to use Isis manufacturing services for RNA-based therapeutic products. In addition, under the Isis agreement, we have the exclusive right to grant sub-licenses for Isis technology to third parties with whom we are not collaborating. We may include these sub-licenses in our non-exclusive platform licenses and our InterfeRx licenses. If a license includes rights to Isis intellectual property, we will share revenues from that license equally with Isis.

Novartis. We have formed two alliances with Novartis. We refer to the first of these, which was initiated in September 2005, as the broad Novartis alliance, and to the second, which was initiated in February 2006, as the Novartis flu alliance.

In connection with the broad Novartis alliance, we entered into a series of transactions with Novartis beginning in September 2005. At that time, we and Novartis executed a stock purchase agreement and an investor rights agreement. When the transactions contemplated by the stock purchase agreement closed in October 2005, the investor rights agreement became effective and we and Novartis executed a research collaboration and license agreement. The collaboration and license agreement had an initial term of three years, with an option for two additional one-year extensions at the election of Novartis. In July 2008, Novartis elected to extend the initial term for an additional year, through October 2009. Novartis retains the right to extend the term for a second additional year, which right must be exercised no later than July 2009.

Under the terms of the collaboration and license agreement, the parties will work together on selected targets, as defined in the collaboration and license agreement, to discover and develop therapeutics based on RNAi. In consideration for rights granted to Novartis under the collaboration and license agreement, Novartis made an upfront payment of $10.0 million to us in October 2005, partly to reimburse prior costs incurred by us to develop *in vivo* RNAi technology. The collaboration and license agreement also includes terms under which Novartis will provide us with research funding and development and sales milestone payments as well as royalties on annual net sales of products resulting from the collaboration, if any. The amount of research funding provided by Novartis under the collaboration and license agreement during the research term is dependent upon the number of active programs on which we are collaborating with them at any given time and the number of our employees that are working on those programs, in respect of which Novartis reimburses us at an agreed upon rate. Under the terms of the collaboration and license agreement, Novartis has the right to select up to 30 exclusive targets to include in the collaboration, which number may be increased to 40 under certain circumstances and upon additional payments. For RNAi therapeutic products successfully developed under the agreement, if any, we would be entitled to receive milestone payments upon achievement of certain specified development and annual net sales events, up to an aggregate of $75.0 million per therapeutic product. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any milestone or royalty payments from Novartis.

The collaboration and license agreement also provides Novartis with a non-exclusive option to integrate into its operations our intellectual property relating to RNAi technology, excluding any technology related to delivery of nucleic acid based molecules. Novartis may exercise this integration option at any point during the research term, as defined in the collaboration and license agreement. The research term expires in October 2009 and may be extended until October 2010 at Novartis election. In connection with the exercise of the integration option, Novartis would be required to make additional payments to us totaling $100.0 million, payable in full at the time of exercise, which payments would include an option exercise fee, a milestone based on the overall success of the collaboration and pre-paid milestones and royalties that could become due as a result of future development of products using our technology. In addition, under this license grant, Novartis may be required to make milestone and royalty payments to us in connection with the successful development and commercialization of RNAi therapeutic products, if any. The license grant under the integration option, if exercised by Novartis, would be structured similarly to our non-exclusive platform licenses with Roche and Takeda.

Under the terms of the stock purchase agreement, in October 2005, Novartis purchased 5,267,865 shares of our common stock at a purchase price of $11.11 per share for an aggregate purchase price of $58.5 million, which, after such issuance, represented 19.9% of our outstanding common stock as of the date of issuance. In addition, under the investor rights agreement, we granted Novartis rights to acquire additional equity securities in the event that we propose to sell or issue any equity securities, subject to specified exceptions, as described in the investor rights agreement, such that Novartis would be able to maintain its then-current ownership percentage in our outstanding common stock. Pursuant to terms of the investor rights agreement, in May 2008, Novartis purchased 213,888 shares of our common stock at a purchase price of $25.29 per share resulting in a payment to us of $5.4 million. At December 31, 2008, Novartis owned 13.2% of our outstanding common stock.

In February 2006, we entered into the Novartis flu alliance. Under the terms of the Novartis flu alliance, we and Novartis have joint responsibility for the development of RNAi therapeutics for pandemic flu. This program was stopped and currently there are no specific resource commitments for this program.

Biogen Idec. In September 2006, we entered into a collaboration and license agreement with Biogen Idec. The collaboration is focused on the discovery and development of therapeutics based on RNAi for the potential treatment of PML. Under the terms of the Biogen Idec agreement, we granted Biogen Idec an exclusive license to distribute, market and sell certain RNAi therapeutics to treat PML and Biogen Idec has agreed to fund all related research and development activities. We received an upfront $5.0 million payment from Biogen Idec. In addition, upon the successful development and utilization of a product resulting from the collaboration, if any, Biogen Idec would be required to pay us milestone payments, totaling $51.0 million, and royalty payments on sales, if any. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any milestone or royalty payments from Biogen Idec. The pace and scope of future development of this program is the responsibility of Biogen Idec. We expect to expend limited resources on this program in 2009.

Product Alliances.

Medtronic. In July 2007, we entered into an amended and restated collaboration agreement with Medtronic to pursue the development of therapeutic products for the treatment of neurodegenerative disorders. The amended and restated collaboration agreement supersedes the collaboration agreement entered into by the parties in February 2005, and continues the existing collaboration between the parties focusing on the delivery of RNAi therapeutics to specific areas of the brain using implantable infusion systems.

Under the terms of the amended and restated collaboration agreement, we and Medtronic are continuing our existing development program focused on developing a combination drug-device product for the treatment of Huntington s disease. In addition, we and Medtronic may jointly agree to collaborate on additional product development programs for the treatment of other neurodegenerative diseases, which can be addressed by the delivery of siRNAs discovered and developed using our RNAi therapeutics platform to the human nervous system through implantable infusion devices developed by Medtronic. We will be responsible for supplying the siRNA component and Medtronic will be responsible for supplying the device component of any product resulting from the collaboration.

With respect to the initial product development program focused on Huntington s disease, each party is funding 50% of the development efforts for the United States while Medtronic is responsible for funding development efforts outside the United States. Medtronic will commercialize any resulting products and pay royalties to us based on net sales of any such products, if any, which royalties in the United States are designed to approximate 50% of the profit associated with the sale of such product and which royalties in Europe are similar to more traditional pharmaceutical royalties, in that they are intended to reflect each party s contribution.

Each party has the right to opt out of its obligation to fund the program under the agreement at certain stages, and the agreement provides for revised economics based on the timing of any such opt out. Other than pursuant to the initial product development program, and subject to specified exceptions, neither party may research, develop, manufacture or commercialize products that use implanted infusion devices for the direct delivery of siRNAs to the human nervous system to treat Huntington s disease during the term of such program.

Kyowa Hakko. In June 2008, we entered into a license and collaboration agreement with Kyowa Hakko. Under the Kyowa Hakko agreement, we granted Kyowa Hakko an exclusive license to our intellectual property in Japan and other markets in Asia for the development and commercialization of ALN-RSV01 for the treatment of RSV infection. The Kyowa Hakko agreement also covers additional RSV-specific RNAi therapeutic compounds that comprise the ALN-RSV program. We retain all development and commercialization rights worldwide excluding the licensed territory.

Under the terms of the Kyowa Hakko agreement, in June 2008, Kyowa Hakko paid us an upfront cash payment of $15.0 million. In addition, Kyowa Hakko is required to make payments to us upon achievement of specified development and sales milestones totaling up to $78.0 million, and royalty payments based on annual net sales, if any, of ALN-RSV01 by Kyowa Hakko, its affiliates and sublicensees in the licensed territory. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any milestone or royalty payments from Kyowa Hakko.

Our collaboration with Kyowa Hakko is governed by a joint steering committee that is comprised of an equal number of representatives from each party. Under the agreement, Kyowa Hakko is establishing a development plan for ALN-RSV01 relating to the development activities to be undertaken in the licensed territory, with the initial focus on Japan. Kyowa Hakko is responsible, at its expense, for all development activities under the development plan that are reasonably necessary for the regulatory approval and commercialization of ALN-RSV01 in Japan and the rest of the licensed territory. We will be responsible for supply of the product to Kyowa Hakko under a supply agreement unless Kyowa Hakko elects, prior to the first commercial sale of the product in the licensed territory, to manufacture the product itself or arrange for a third party to manufacture the product.

Cubist. In January 2009, we entered into a license and collaboration agreement with Cubist to develop and commercialize therapeutic products based on certain of our RNAi technology for the treatment of RSV, including ALN-RSV01, which is currently in Phase II clinical development for the treatment of RSV infection in adult lung transplant patients, as well as several other second-generation RNAi-based RSV inhibitors, which currently are in pre-clinical studies.

Under the terms of the Cubist agreement, we and Cubist will share responsibility for developing licensed products in North America and will each bear one-half of the related development costs. Our collaboration with Cubist for the development of licensed products in North America will be governed by a joint steering committee comprised of an equal number of representatives from each party. Cubist will have the sole right to commercialize licensed products in North America with costs associated with such activities and any resulting profits or losses to be split equally between us and Cubist. Throughout the rest of the world, referred to as the Royalty Territory, excluding Asia, where we have previously partnered our ALN-RSV program with Kyowa Hakko, Cubist will have an exclusive, royalty-bearing license to develop and commercialize licensed products.

In consideration for the rights granted to Cubist under the agreement, in January 2009, Cubist paid us an upfront cash payment of $20.0 million. Cubist also has an obligation under the agreement to pay us milestone payments, totaling up to an aggregate of $82.5 million, upon the achievement of specified development and sales events in the Royalty Territory. In addition, if licensed products are successfully developed, Cubist will be required to pay us double digit royalties on net sales of licensed products in the Royalty Territory, if any, subject to offsets under certain circumstances. Upon achievement of certain development milestones, we will have the right to convert the North American co-development and profit sharing arrangement into a royalty-bearing license and, in addition to royalties on net sales in North America, will be entitled to receive additional milestone payments totaling up to an aggregate of $130.0 million upon achievement of specified development and sales events in North America, subject to the timing of the conversion by us and the regulatory status of a licensed product at the time of conversion. If we make the conversion to a royalty-bearing license with respect to North America, then North America becomes part of the Royalty Territory. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, we may not receive any milestone or royalty payments from Cubist.

Delivery Initiatives

We are working to extend our capabilities in developing technology to achieve effective and safe delivery of RNAi therapeutics to a broad spectrum of organ and tissue types. In connection with these efforts, we have entered into a number of agreements to evaluate and gain access to certain delivery technologies. In some instances, we are also providing funding to support the advancement of these delivery technologies.

For example, in May of 2007, we entered into an agreement with the MIT, Center for Cancer Research under which we are sponsoring an exclusive five-year research program focused on the delivery of RNAi therapeutics. In addition, during 2007, we obtained an exclusive worldwide license to the liposomal delivery formulation technology of Tekmira for the discovery, development and commercialization of lipid-based nanoparticle formulations for the delivery of RNAi therapeutics. In May 2008, Tekmira acquired Protiva Biotherapeutics Inc., or Protiva. In connection with this acquisition, we entered into new agreements with Tekmira and Protiva, which provide us access to key existing and future technology and intellectual property for the systemic delivery of RNAi therapeutics with liposomal delivery technologies. Under the new agreements with Tekmira and Protiva, we continue to have exclusive rights to the Semple (U.S. Patent No. 6,858,225) and Wheeler (U.S. Patent Nos. 5,976,567 and 6,815,432) patents for RNAi, which we believe are critical for the use of cationic liposomal delivery technology.

As noted above, we are developing ALN-VSP, a systemically delivered RNAi therapeutic candidate, for the treatment of liver cancers, including hepatocellular carcinoma and other solid tumors with liver involvement. ALN-VSP comprises two siRNAs formulated using Tekmira s stable nucleic acid-lipid particles, or SNALP, technology. We also have rights to use SNALP technology in the advancement of our other systemically delivered RNAi therapeutic programs, including ALN-PCS for the treatment of hypercholesterolemia and ALN-TTR for the treatment of TTR amyloidosis.

In connection with Tekmira s acquisition of Protiva, in May 2008 we made an equity investment of $5.0 million in Tekmira, purchasing 2,083,333 shares of Tekmira common stock at a price of $2.40 per share, which represented a premium of $1.00 per share, or an aggregate of $2.1 million. This premium was calculated on the difference between the purchase price and the closing price of Tekmira s common stock on the effective date of the acquisition. We allocated this $2.1 million premium to the expansion of our access to key technology and intellectual property rights and, accordingly, recorded a charge to research and development expense during the year ended December 31, 2008. During 2008, we recorded an impairment charge of $1.6 million related to our investment in Tekmira, as the decrease in the fair value of this investment was deemed to be other than temporary. In connection with these transactions, we and Tekmira cancelled our $5.0 million capital equipment loan to Tekmira, which was never drawn down by Tekmira.

We have other RNAi therapeutic delivery collaborations and intend to continue to collaborate with government, academic and corporate third parties to evaluate different delivery technologies, including with respect to Direct RNAi and Systemic RNAi.

Government Funding

NIH. In September 2006, NIAID awarded us a contract for up to $23.0 million over four years to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus, including the Ebola virus. The Ebola virus can cause a severe, often fatal infection, and poses a potential biological safety risk and bioterrorism threat. Of the $23.0 million in funding, the government initially committed to pay us up to $14.2 million over the first two years of the contract. In June 2008, as a result of the progress of the program, the government awarded us an additional $7.5 million, to be paid through September 2009 for the third year of the contract, together with any remaining funds carried over from the funding allocated for the first two years of the contract.

Department of Defense. In August 2007, DTRA awarded us a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus. The government initially committed to pay us up to $10.9 million through February 2009, which included a six-month extension granted by DTRA in July 2008. Following a program review in early 2009, we and DTRA have determined to end this program and accordingly, the remaining funds of up to $27.7 million will not be accessed.

microRNAi-based Therapeutics

Regulus Therapeutics. In September 2007, we and Isis established Regulus Therapeutics, a company focused on the discovery, development and commercialization of microRNA-based therapeutics. Regulus Therapeutics combines our and Isis technologies, know-how and intellectual property relating to microRNA-based therapeutics. Since microRNAs are believed to regulate the expression of broad networks of genes and biological pathways, microRNA-based therapeutics define a new and potentially high-impact strategy to target multiple points on disease pathways. Regulus Therapeutics, which had initially been established as a limited liability company, converted to a C corporation as of January 2, 2009 and changed its name to Regulus Therapeutics Inc.. We and Isis continue to own 49% and 51%, respectively, of Regulus Therapeutics. Regulus Therapeutics continues to operate as an independent company with a separate board of directors, scientific advisory board and management team.

Regulus Therapeutics most advanced program, which is in pre-clinical research, is a microRNA-based therapeutic candidate that targets miR-122, an endogenous host gene required for viral infection by the hepatitis C virus, or HCV. HCV infection is a significant disease worldwide, for which emerging therapies target viral genes and, therefore, are prone to viral resistance. Regulus Therapeutics is also pursuing a program that targets miR-21. Pre-clinical studies by

Regulus Therapeutics and collaborators have shown that miR-21 is implicated in several therapeutic areas, including heart failure and fibrosis. In addition to these programs, Regulus Therapeutics is also actively exploring additional areas for development of microRNA-based therapeutics, including cancer, other viral diseases, metabolic disorders and inflammatory diseases.

In April 2008, Regulus Therapeutics entered into a worldwide strategic alliance with GlaxoSmithKline, or GSK, to discover, develop and market novel microRNA-targeted therapeutics to treat inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. In connection with this alliance, Regulus Therapeutics received $20.0 million in upfront payments from GSK, including a $15.0 million option fee and a loan of $5.0 million evidenced by a promissory note (guaranteed by Isis and us) that will convert into Regulus Therapeutics common stock under certain specified circumstances. Regulus Therapeutics could be eligible to receive development, regulatory and sales milestone payments for each of the four microRNA-targeted therapeutics discovered and developed as part of the alliance, and would also receive royalty payments on worldwide sales of products resulting from the alliance, if any.

Critical Accounting Policies and Estimates

Our discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of our consolidated financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses and disclosure of contingent liabilities in our consolidated financial statements. Actual results may differ from these estimates under different assumptions or conditions and could have a material impact on our reported results. While our significant accounting policies are more fully described in the Notes to our consolidated financial statements included elsewhere in this annual report on Form 10-K, we believe the following accounting policies to be the most critical in understanding the judgments and estimates we use in preparing our consolidated financial statements:

Revenue Recognition

Our business strategy includes entering into collaborative license and development agreements with biotechnology and pharmaceutical companies for the development and commercialization of our product candidates. The terms of the agreements typically include non-refundable license fees, funding of research and development, payments based upon achievement of clinical and pre-clinical development milestones and royalties on product sales. We follow the provisions of the Securities and Exchange Commission s Staff Accounting Bulletin No. 104, Revenue Recognition, Emerging Issues Task Force, or EITF, Issue No. 00-21, Accounting for Revenue Arrangements with Multiple Deliverables, or EITF 00-21, EITF Issue No. 99-19, Reporting Revenue Gross as a Principal Versus Net as an Agent, and EITF Issue No. 01-9, Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor s Products), or EITF 01-9.

Non-refundable license fees are recognized as revenue upon delivery of the license only if we have a contractual right to receive such payment, the contract price is fixed or determinable, the collection of the resulting receivable is reasonably assured and we have no further performance obligations under the license agreement. Multiple element arrangements, such as license and development arrangements, are analyzed to determine whether the deliverables, which often include a license and performance obligations such as research and steering committee services, can be separated or whether they must be accounted for as a single unit of accounting in accordance with EITF 00-21. We recognize upfront license payments as revenue upon delivery of the license only if the license has stand-alone value and the fair value of the undelivered performance obligations, typically including research and/or steering committee services, can be determined. If the fair value of the undelivered performance obligations can be determined, such obligations would then be accounted for separately as performed. If the license is considered to either not have stand-alone value or have stand-alone value but the fair value of any of the undelivered performance obligations cannot be determined, the arrangement would then be accounted for as a single unit of accounting and the license payments and payments for performance obligations are recognized as revenue over the estimated period of when the performance obligations are performed.

Whenever we determine that an arrangement should be accounted for as a single unit of accounting, we must determine the period over which the performance obligations will be performed and revenue will be recognized. Revenue will be recognized using either a proportional performance or straight-line method. We recognize revenue using the proportional performance method when we can reasonably estimate the level of effort required to complete our performance obligations under an arrangement and such performance obligations are provided on a best-efforts basis. Direct labor hours or full-time equivalents are typically used as the measure of performance.

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Revenue recognized under the proportional performance method would be determined by multiplying the total payments under the contract, excluding royalties and payments contingent upon achievement of substantive milestones, by the ratio of level of effort incurred to date to estimated total level of effort required to complete our performance obligations under the arrangement. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the proportional performance method, as of the period ending date.

If we cannot reasonably estimate the level of effort required to complete our performance obligations under an arrangement, then revenue under the arrangement will be recognized as revenue on a straight-line basis over the period we expect to complete our performance obligations. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method, as of the period ending date.

Significant management judgment is required in determining the level of effort required under an arrangement and the period over which we are expected to complete our performance obligations under an arrangement. Steering committee services that are not inconsequential or perfunctory and that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort required in an arrangement and the period over which we expect to complete our aggregate performance obligations.

Many of our collaboration agreements entitle us to additional payments upon the achievement of performance-based milestones. If the achievement of a milestone is considered probable at the inception of the collaboration, the related milestone payment is included with other collaboration consideration, such as up-front fees and research funding, in our revenue model. Milestones that involve substantial effort on our part and the achievement of which are not considered probable at the inception of the collaboration are considered substantive milestones. Substantive milestones are included in our revenue model when achievement of the milestone is considered probable. As future substantive milestones are achieved, a portion of the milestone payment, equal to the percentage of the performance period completed when the milestone is achieved, multiplied by the amount of the milestone payment, will be recognized as revenue upon achievement of such milestone. The remaining portion of the milestone will be recognized over the remaining performance period using the proportional performance or straight-line method. Milestones that are tied to regulatory approval are not considered probable of being achieved until such approval is received. Milestones tied to counter-party performance are not included in our revenue model until the performance conditions are met.

For revenue generating arrangements where we, as a vendor, provide consideration to a licensor or collaborator, as a customer, we apply the provisions of EITF 01-9. EITF 01-9 addresses the accounting for revenue arrangements where both the vendor and the customer make cash payments to each other for services and/or products. A payment to a customer is presumed to be a reduction of the selling price unless we receive an identifiable benefit for the payment and we can reasonably estimate the fair value of the benefit received. Payments to a customer that are deemed a reduction of selling price are recorded first as a reduction of revenue, to the extent of both cumulative revenue recorded to date and probable future revenues, which include any unamortized deferred revenue balances, under all arrangements with such customer, and then as an expense. Payments that are not deemed to be a reduction of selling price would be recorded as an expense.

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized within the next twelve months are classified as long-term deferred revenue. As of December 31, 2008, we had short-term and long-term deferred revenue of $79.9 million and $250.1 million, respectively, related to our collaborations.

Although we follow detailed guidelines in measuring revenue, certain judgments affect the application of our revenue policy. For example, in connection with our existing collaboration agreements, we have recorded on our balance sheet short-term and long-term deferred revenue based on our best estimate of when such revenue will be recognized. Short-term deferred revenue consists of amounts that are expected to be recognized as revenue in the next twelve months. Amounts that we expect will not be recognized prior to the next twelve months are classified as long-term deferred revenue. However, this estimate is based on our current operating plan and, if our operating plan should change in the future, we may recognize a different amount of deferred revenue over the next twelve-month period.

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The estimate of deferred revenue also reflects management s estimate of the periods of our involvement in certain of our collaborations. Our performance obligations under these collaborations consist of participation on steering committees and the performance of other research and development services. In certain instances, the timing of satisfying these obligations can be difficult to estimate. Accordingly, our estimates may change in the future. Such changes to estimates would result in a change in revenue recognition amounts. If these estimates and judgments change over the course of these agreements, it may affect the timing and amount of revenue that we recognize and record in future periods.

Novartis. In consideration for rights granted to Novartis under the collaboration and license agreement, Novartis made an up-front payment of $10.0 million to us in October 2005 to partly reimburse costs previously incurred by us to develop *in vivo* RNAi technology. The collaboration and license agreement includes terms under which Novartis will provide us with research funding. In addition, for RNAi therapeutic products successfully developed under the agreement, if any, we would be entitled to receive milestone payments upon achievement of certain specified development and annual net sales events, up to an aggregate of $75.0 million per therapeutic product. We initially recorded as deferred revenue the non-refundable $10.0 million up-front payment and $6.4 million premium that represents the difference between the purchase price and the closing price of our common stock on the date of the stock purchase from Novartis. In addition to these payments, research funding and certain milestone payments, the receipt of which is considered probable, are being amortized into revenue using the proportional performance method over the estimated duration of the Novartis agreement, or ten years. We only include milestone payments that we believe are probable of being received. Under this method, we estimate the level of effort to be expended over the term of the agreement and recognize revenue based on the lesser of the amount calculated based on the proportional performance of total expected revenue or the amount of non-refundable payments earned. As future substantive milestones are achieved, and to the extent they are within the period of performance, milestone payments will be recognized as revenue on a proportional performance basis over the contract s entire performance period, starting with the contract s commencement. A portion of the milestone payment, equal to the percentage of total performance completed when the milestone is achieved, multiplied by the milestone payment, will be recognized as revenue upon achievement of the milestone. The remaining portion of the milestone will be recognized over the remaining performance period under the proportional performance method.

We believe our estimated period of performance under the Novartis agreement includes the three-year term of the agreement, two one-year extensions at the election of Novartis and limited support as part of a technology transfer until the fifth anniversary of the termination of the agreement. In July 2008, Novartis elected to extend the initial term of the agreement for an additional year, through October 2009. We continue to use an expected term of ten years in our proportional performance model. We reevaluate the expected term when new information is known that could affect our estimate. In the event our period of performance is different than we estimated, revenue recognition will be adjusted on a prospective basis.

Roche. We recorded $278.2 million as deferred revenue in connection with the Roche alliance. This amount represents the aggregate proceeds received from Roche of $331.0 million, net of the amount allocated for financial statement purposes to the common stock issuance of $51.3 million and the net book value of Alnylam Europe of $1.5 million. In exchange for our contributions under the collaboration agreement, for each RNAi therapeutic product successfully developed by Roche, its affiliates or sublicensees under the collaboration agreement, if any, we are entitled to receive milestone payments upon achievement of specified development and sales events, totaling up to an aggregate of $100.0 million per therapeutic target, together with royalty payments based on worldwide annual net sales, if any. In addition, we have agreed with Roche to collaborate on the discovery of RNAi therapeutic products directed to one or more disease targets, referred to as the Discovery Collaboration, subject to our existing contractual obligations to third parties. The collaboration between Roche and us will be governed by a joint steering committee for a period of five years that is comprised of an equal number of representatives from each party. Our performance obligations under the license and collaboration agreement, including participation in the steering committee and research conducted as part of the Discovery Collaboration, are expected to cease five years from the effective date of the license and collaboration agreement.

The proceeds allocated to the common stock issuance of $51.3 million were based on the fair value on the date the shares were issued. We have concluded that the license issued to Roche, the Alnylam Europe assets and employees, the steering committee services and the services we will be required to perform under the Discovery

Collaboration should be treated as a single unit of accounting. Accordingly, the remaining consideration received has been recorded as deferred revenue and will be amortized into revenue over the five-year period during which we are required to provide services under the license and collaboration agreement. We are recognizing revenue on a straight-line basis over five years because we are unable to reasonably estimate the total level of effort required under the license and collaboration agreement. When, and if, we are able to make a reasonable estimate of our remaining efforts under the collaboration, we will modify the method of recognition and utilize the proportional performance method. As future substantive milestones are achieved, a portion of the milestone payment, equal to the percentage of the performance period completed when the milestone is achieved, multiplied by the amount of the milestone payment, will be recognized as revenue upon achievement of such milestone. The remaining portion of the milestone will be recognized over the remaining performance period on a straight-line basis.

Takeda. In consideration for the rights granted to Takeda under the Takeda agreement, Takeda agreed to pay us $150.0 million in upfront and near-term technology transfer payments. In June 2008, Takeda paid us an upfront payment of $100.0 million. Takeda is also required to make an additional $50.0 million in payments to us upon achievement of specified technology transfer milestones, $20.0 million of which was paid in October 2008, $20.0 million of which is required to be paid within 12 to 24 months of execution of the agreement and $10.0 million of which is required to be paid within 24 to 36 months of execution of the agreement. If Takeda elects to expand its license to additional therapeutic areas, Takeda will be required to pay us $50.0 million for each of up to approximately 20 total additional fields selected, comprising all other fields of human disease, as identified and agreed upon by the parties. In addition, for each RNAi therapeutic product successfully developed by Takeda, its affiliates and sublicensees, if any, we are entitled to receive specified development and commercialization milestones, totaling up to $171.0 million per product, together with royalty payments based on worldwide annual net sales, if any.

Pursuant to the Takeda agreement, we and Takeda have also agreed to collaborate on the research of RNAi therapeutics directed to one or two disease targets agreed to by the parties, subject to our existing contractual obligations with third parties. Takeda also has the option, subject to certain conditions, to collaborate with us on the research and development of RNAi drug delivery technology for targets agreed to by the parties. In addition, Takeda has a right of first negotiation for the development and commercialization of our RNAi therapeutic products in the Asian territory, excluding our ALN-RSV01 program. In addition to our 50-50 profit sharing option, we have a similar right of first negotiation to participate with Takeda in the development and commercialization in the United States of licensed products. The collaboration is governed by a joint technology transfer committee, or JTTC, a joint research collaboration committee, or JRCC, and a joint delivery collaboration committee, or JDCC, each of which is comprised of an equal number of representatives from each party.

We have determined that the deliverables under the Takeda agreement include the license, the joint committees (the JTTC, JRCC and JDCC), the technology transfer activities and the services that we will be obligated to perform under the research collaboration with Takeda. We have determined that, pursuant to EITF 00-21, the license and undelivered services (i.e., the joint committees and the research collaboration) are not separable and, accordingly, the license and services are being treated as a single unit of accounting. Under the Takeda agreement, the last elements to be delivered are the JDCC and JTTC services, each of which has a life of no more than seven years. We are initially recognizing the upfront payment of $100.0 million, the first technology transfer milestone of $20.0 million and the $30.0 million of remaining technology transfer milestones, the receipt of which we believe is probable, on a straight-line basis over seven years because we are unable to reasonably estimate the level of effort to fulfill these obligations, primarily because the effort required under the research collaboration is largely unknown. As future substantive milestones are achieved, a portion of the milestone payment, equal to the percentage of the performance period completed when the milestone is achieved, multiplied by the amount of the milestone payment, will be recognized as revenue upon achievement of such milestone. The remaining portion of the milestone will be recognized over the remaining performance period on a straight-line basis. We will continue to reassess whether we can reasonably estimate the level of effort required to fulfill our obligations under the Takeda agreement. When, and if, we can make a reasonable estimate of our remaining efforts under the collaboration, we would modify our method of recognition and utilize a proportional performance method.

Kyowa Hakko. Under the terms of the Kyowa Hakko agreement, in June 2008, Kyowa Hakko paid us an upfront cash payment of $15.0 million. In addition, Kyowa Hakko is required to make payments to us upon achievement of specified development and sales milestones totaling up to $78.0 million, and royalty payments based on annual net sales, if any, of ALN-RSV01 by Kyowa Hakko, its affiliates and sublicenses in the licensed territory.

Our collaboration with Kyowa Hakko is governed by a joint steering committee that is comprised of an equal number of representatives from each party. Kyowa Hakko is responsible, at its expense, for all development activities under the development plan that are reasonably necessary for the regulatory approval and commercialization of ALN-RSV01 in Japan and the rest of the licensed territory. We will be responsible for supply of the product to Kyowa Hakko under a supply agreement unless Kyowa Hakko elects, prior to the first commercial sale of the product in the licensed territory, to manufacture the product itself or arrange for a third party to manufacture the product.

We have determined that the deliverables under the Kyowa Hakko agreement include the license, the joint steering committee, the manufacturing services and any additional RSV-specific RNAi therapeutic compounds that comprise the ALN-RSV program. We have determined that pursuant to EITF 00-21, the individual deliverables are not separable and, accordingly, must be accounted for as a single unit of accounting. We are currently unable to reasonably estimate our period of performance under the Kyowa Hakko agreement, as we are unable to estimate the timeline of our deliverables related to the fixed-price option granted to Kyowa Hakko for any additional compounds. We are deferring all revenue under the Kyowa Hakko agreement until we are able to reasonably estimate our period of performance. We will continue to reassess whether we can reasonably estimate the period of performance to fulfill our obligations under the Kyowa Hakko agreement.

Government Contracts. Revenue under government cost reimbursement contracts is recognized as we perform the underlying research and development activities.

Accounting for Income Taxes

Effective January 1, 2007, we adopted the provisions of Financial Accounting Standards Board, or FASB, Interpretation No. 48, Accounting for Uncertainty in Income Taxes an interpretation of FASB Statement 109, or FIN 48, which clarifies the accounting for income tax positions by prescribing a minimum recognition threshold that a tax position is required to meet before being recognized in the financial statements. FIN 48 also provides guidance on the derecognition of previously recognized deferred tax items, measurement, classification, interest and penalties, accounting in interim periods, disclosure and transition. Under FIN 48, we recognize the tax benefit from an uncertain tax position only if it is more likely than not that the tax position will be sustained upon examination by the taxing authorities, based on the technical merits of the tax position. The tax benefits recognized in our financial statements from such a position are measured based on the largest benefit that has a greater than 50% likelihood of being realized upon ultimate resolution.

We operate in the United States and Germany where our income tax returns are subject to audit and adjustment by local tax authorities. The nature of the uncertain tax positions is often very complex and subject to change and the amounts at issue can be substantial. We develop our cumulative probability assessment of the measurement of uncertain tax positions using internal experience, judgment and assistance from professional advisors. Estimates are refined as additional information becomes known. Any outcome upon settlement that differs from our current estimate may result in additional tax expense in future periods.

We recognize income taxes when transactions are recorded in our consolidated statements of operations, with deferred taxes provided for items that are recognized in different periods for financial statement and tax reporting purposes. We record a valuation allowance to reduce the deferred tax assets to the amount that is more likely than not to be realized. In addition, we estimate our exposures relating to uncertain tax positions and establish reserves for such exposures when they become probable and reasonably estimable.

For the years ended December 31, 2008 and 2007, we recorded a provision for income taxes of $0.7 million and $5.2 million, respectively. We provide income tax expense for federal alternative minimum tax, state and foreign taxes. We generated U.S. taxable income during 2008 due to the recognition of certain proceeds received from the Roche alliance. Our 2008 U.S. taxable income will be offset by net operating loss carry forwards and other deferred tax attributes. However, we anticipate being subject to federal alternative minimum tax and state income taxes.

At December 31, 2008, we had a valuation allowance against our net deferred tax assets to the extent it is more likely than not that the assets will not be realized. At December 31, 2008, we had utilized all federal and Massachusetts state net operating loss carryforwards and all federal and a significant portion of Massachusetts state research and development credits and all foreign tax credits. At December 31, 2008, we had $0.5 million of state research and development credits remaining and $8.6 million of California net operating losses. We have placed a valuation allowance against the state net operating loss and state credit deferred tax assets as it is unlikely that we will realize these assets. Ownership changes, as defined in the Internal Revenue Code, including those resulting from the issuance of common stock in connection with our public offerings, may limit the amount of net operating loss and tax credit carryforwards that can be utilized to offset future taxable income or tax liability. The amount of the limitation is determined in accordance with Section 382 of the Internal Revenue Code. We have determined that there is no limitation on the utilization of net operating loss and tax credit carryforwards in accordance with Section 382 of the Internal Revenue Code in 2008.

Accounting for Stock-Based Compensation

Effective January 1, 2006, we adopted the fair value recognition provisions of FASB Statement of Financial Accounting Standards, or SFAS, No. 123R, Share-Based Payment, an amendment of FASB Statements Nos. 123 and 95, or SFAS 123R, using the modified prospective transition method. All stock-based awards granted to non-employees are accounted for at their fair value in accordance with SFAS No. 123, Accounting for Stock Based Compensation and EITF Issue No. 96-18, Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services, under which compensation expense is generally recognized over the vesting period of the award. Determining the amount of stock-based compensation to be recorded requires us to develop estimates of fair values of stock options as of the grant date. We calculate the grant date fair values using the Black-Scholes valuation model. Our expected stock price volatility assumption is based on a combination of the historical and implied volatility of our publicly traded stock. For stock option grants issued during the year ended December 31, 2008, we used a weighted-average expected stock-price volatility assumption of 66%. Our expected life assumption is based on the equal weighting of our historical data and the historical data of our pharmaceutical and biotechnology peers. Our weighted average expected term was 6.1 years for the year ended December 31, 2008. We utilize a dividend yield of zero based on the fact that we have never paid cash dividends and have no present intention to pay cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life.

As of December 31, 2008, the estimated fair value of unvested employee awards was $50.0 million, net of estimated forfeitures. This amount will be recognized over the weighted average remaining vesting period of approximately 1.6 years for these awards. Stock-based employee compensation expense was $16.4 million for the year ended December 31, 2008. However, the total amount of stock-based compensation expense recognized in any future period cannot be predicted at this time because it will depend on levels of stock-based payments granted in the future as well as the portion of the awards that actually vest. SFAS 123R requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The term forfeitures is distinct from cancellations or expirations and represents only the unvested portion of the surrendered option. We currently expect, based on an analysis of our historical forfeitures, that approximately 86% of our options will actually vest, and therefore have applied an annual forfeiture rate of 3.7% to all unvested options as of December 31, 2008. Ultimately, the actual expense recognized over the vesting period will only be for those shares that vest.

Accounting for Joint Venture

We account for our interest in Regulus Therapeutics using the equity method of accounting. We have concluded that Regulus Therapeutics qualifies as a variable interest entity under FASB Interpretation No. 46R, Consolidation of Variable Interest Entities an interpretation of Accounting Research Bulletin No. 51, or FIN 46R. The limited liability company agreement contains transfer restrictions on each of Isis and our interests and, as a result, we and Isis are considered related parties under paragraph 16(d)(1) of FIN 46R. Because we and Isis are related parties and collectively own 100% of Regulus Therapeutics, the determination of which entity would be considered the primary beneficiary is based on which entity is most closely associated with Regulus Therapeutics.

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Following the guidance in paragraph 17 of FIN 46R, we have concluded that Isis is the primary beneficiary and, accordingly, we have not consolidated Regulus Therapeutics and account for our investment under the equity method of accounting.

Results of Operations

The following data summarizes the results of our operations for the periods indicated, in thousands:

	Year Ended December 31,		
	2008	**2007**	**2006**
Net revenues	$ 96,163	$ 50,897	$ 26,930
Operating expenses	123,998	144,074	66,431
Loss from operations	(27,835)	(93,177)	(39,501)
Net loss	$ (26,249)	$ (85,466)	$ (34,608)

Discussion of Results of Operations for 2008 and 2007

The following table summarizes our total consolidated net revenues from research collaborators, for the periods indicated, in thousands:

	Year Ended December 31,	
	2008	**2007**
Roche	$ 54,427	$ 17,571
Government contract	14,172	9,800
Takeda	12,794	
Novartis	11,635	14,670
InterfeRx program, research reagent license and other	2,207	1,526
Other research collaborator	928	7,330
Total net revenues from research collaborators	$ 96,163	$ 50,897

Revenues increased significantly for the year ended December 31, 2008 as compared to the year ended December 31, 2007 primarily as a result of our August 2007 alliance with Roche, as well as our May 2008 alliance with Takeda. Under the Roche alliance, $278.2 million is being recognized as revenue on a straight-line basis over five years, which equates to approximately $14.0 million per quarter. In connection with the Roche alliance, Roche Kulmbach employees performed certain transition services for us at various levels through August 2008. We reimbursed Roche for these services at an agreed-upon rate. We recorded as contra revenue (a reduction of revenues) $1.0 million and $4.2 million for these services during the years ended December 31, 2008 and 2007, respectively. Under the Takeda alliance, the $150.0 million in upfront and technology transfer milestone payments made or due to us are being recognized as revenue on a straight-line basis over seven years, which equates to approximately $5.0 million per quarter.

For the year ended December 31, 2008 as compared to the year ended December 31, 2007, government contract revenues increased primarily as a result of our collaboration with DTRA, which began in the third quarter of 2007. Following a program review in early 2009, we and DTRA have determined to end this program after February 2009 and accordingly, no additional funds will be accessed.

The increase in InterfeRx program, research reagent licenses and other revenues for the year ended December 31, 2008 compared to the prior year was due to milestone payments from certain InterfeRx licensees.

The decrease in Novartis revenues during the year ended December 31, 2008 as compared to the year ended December 31, 2007 was due in part to the wind down of the Novartis flu alliance.

Other research collaborator revenues decreased in the year ended December 31, 2008 as compared to the year ended December 31, 2007 due primarily to our termination of the Merck collaboration agreement in September 2007. We were recognizing the remaining deferred revenue under the Merck agreement on a straight-line basis over the remaining period of expected performance of four years. As a result of the termination, we recognized an aggregate of $3.5 million during the third quarter of 2007, which represented all of the remaining deferred revenue under the Merck agreement. In addition, during 2008, we reduced the number of resources allocated to, and received lower external expense reimbursement under, our collaboration with Biogen Idec. The pace and scope of future development under this collaboration is the responsibility of Biogen Idec. We expect to expend limited resources on this program during 2009.

Total deferred revenue of $330.0 million at December 31, 2008 consists of payments received from collaborators, primarily Roche, Takeda and Kyowa Hakko, that we have yet to recognize pursuant to our revenue recognition policies.

For the foreseeable future, we expect our revenues to continue to be derived primarily from our alliances with Roche, Takeda and Novartis, as well as other strategic alliances, collaborations, government contracts and licensing activities.

Operating Expenses

The following tables summarize our operating expenses for the periods indicated, in thousands and as a percentage of total operating expenses, together with the changes, in thousands and percentages:

	2008	% of Total Operating Expenses	2007	% of Total Operating Expenses	Increase (Decrease) $	%
Research and development	$ 96,883	78%	$ 120,686	84%	$ (23,803)	(20)%
General and administrative	27,115	22%	23,388	16%	3,727	16%
Total operating expenses	$ 123,998	100%	$ 144,074	100%	$ (20,076)	(14)%

Research and development. The following table summarizes the components of our research and development expenses for the periods indicated, in thousands and as a percentage of total research and development expenses, together with the changes, in thousands and percentages:

	2008	% of Expense Category	2007	% of Expense Category	Increase (Decrease) $	%
Research and development						
External services	$ 23,732	24%	$ 18,417	15%	$ 5,315	29%
Compensation and related	17,299	18%	13,201	11%	4,098	31%
Clinical trial and manufacturing	13,342	14%	20,662	17%	(7,320)	(35)%
License fees	12,554	13%	42,207	35%	(29,653)	(70)%
Facilities-related	10,181	11%	8,511	7%	1,670	20%
Non-cash stock-based compensation	9,575	10%	9,363	8%	212	2%
Lab supplies and materials	7,838	8%	6,154	5%	1,684	27%
Other	2,362	2%	2,171	2%	191	9%

Total research and development expenses	$ 96,883	100%	$ 120,686	100%	$ (23,803)	(20)%

Research and development expenses decreased during the year ended December 31, 2008 as compared to the year ended December 31, 2007 due primarily to higher license fees during the prior period consisting of $27.5 million in payments to certain entities, primarily Isis, as a result of our alliance with Roche, a non-cash license fee of $7.9 million and a cash license fee of $0.4 million related to the issuance of our stock to Tekmira during 2007 in connection with our original license agreement with Tekmira, and $6.0 million in payments for drug delivery-related activities. Partially offsetting this decrease was $5.0 million in payments made in 2008 to certain entities, primarily Isis, as a result of the Takeda alliance, as well as a charge of $2.1 million in connection with our new Tekmira license agreement and $3.2 million associated with various intellectual property assets.

Clinical trial and manufacturing expenses decreased during the year ended December 31, 2008 as compared to the year ended December 31, 2007 as a result of higher clinical trial and manufacturing expenses in the prior period in support of our clinical program for RSV, for which we began Phase II trials in June 2007.

Partially offsetting these decreases, external services expenses increased during the year ended December 31, 2008 as compared to the year ended December 31, 2007 as a result of higher expenses related to our government programs, our RSV program and our pre-clinical programs for the treatment of liver cancer and Huntington s disease, as well as higher expenses associated with our drug delivery-related collaborations. In addition, compensation and related, lab supplies and materials, and facilities-related expenses increased during the year ended December 31, 2008 as compared to the prior year due to additional research and development headcount to support our alliances and expanding product pipeline.

We expect to continue to devote a substantial portion of our resources to research and development expenses and we expect that research and development expenses will remain consistent or increase slightly in 2009 as we continue development of our and our collaborators product candidates and focus on drug delivery-related technologies.

We do not track actual costs for most of our research and development programs or our personnel and personnel-related costs on a project-by-project basis because all of our programs are in the early stages of development. In addition, a significant portion of our research and development costs are not tracked by project as they benefit multiple projects or our technology platform. However, our collaboration agreements contain cost-sharing arrangements whereby certain costs incurred under the project are reimbursed. Costs reimbursed under the agreements typically include certain direct external costs and a negotiated full-time equivalent labor rate for the actual time worked on the project. In addition, we are reimbursed under our government contracts for certain allowable costs including direct internal and external costs. As a result, although a significant portion of our research and development expenses are not tracked on a project-by-project basis, we do track direct external costs attributable to, and the actual time our employees worked on, our collaborations and government contracts.

General and administrative. The following table summarizes the components of our general and administrative expenses for the periods indicated, in thousands and as a percentage of total general and administrative expenses, together with the changes, in thousands and percentages:

	2008	% of Expense Category	2007	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
General and administrative						
Consulting and professional services	$ 9,281	34%	$ 8,547	36%	$ 734	9%
Non-cash stock-based compensation	6,807	25%	5,109	22%	1,698	33%
Compensation and related	5,757	21%	4,647	20%	1,110	24%
Facilities-related	2,401	9%	2,486	11%	(85)	(3)%
Insurance	682	3%	654	3%	28	4%
Other	2,187	8%	1,945	8%	242	12%
Total general and administrative expenses	$ 27,115	100%	$ 23,388	100%	$ 3,727	16%

The increase in general and administrative expenses during the year ended December 31, 2008 as compared to the prior year was due primarily to an increase in general and administrative headcount during 2008 to support our growth and higher non-cash stock-based compensation. We expect that general and administrative expenses will remain consistent or increase slightly in 2009.

Other income (expense)

Equity in loss of joint venture was $9.3 million and $1.1 million during the years ended December 31, 2008 and 2007, respectively, and in each year related to our share of the net losses incurred by Regulus Therapeutics, which was formed in September 2007. The increase was a result of Regulus Therapeutics ramping up its operations throughout 2008. Separate financial information for Regulus Therapeutics is included in Exhibit 99.1 to this annual report on Form 10-K.

Interest income was $14.4 million in 2008 as compared to $15.4 million in 2007. The decrease was due to our lower average interest rates during the year ended December 31, 2008, partially offset by higher average cash, cash equivalent and marketable securities balances.

Interest expense was $0.9 million in 2008 as compared to $1.1 million in 2007. Interest expense in each period was related to borrowings under our lines of credit with Oxford Finance Corporation, or Oxford, and Lighthouse Capital Partners V, L.P., or Lighthouse, used to finance capital equipment purchases. In December 2008, we defeased the aggregate outstanding balance under the Oxford and Lighthouse credit lines and expect to have no interest expense in 2009.

Included in other expense during the year ended December 31, 2008 was an impairment charge of $1.6 million related to our May 2008 investment in Tekmira, as the decrease in the fair value of this investment was deemed to be other than temporary.

Our provision for income taxes was $0.7 million for year ended December 31, 2008 primarily as a result of our 2007 alliance with Roche. Income tax expense was $5.2 million for the prior year primarily as a result of the sale of our German operations to Roche in August 2007 for $15.0 million.

Discussion of Results of Operations for 2007 and 2006

The following table summarizes our total consolidated net revenues from research collaborators, for the periods indicated, in thousands:

	Year Ended December 31, 2007	Year Ended December 31, 2006
Roche	$ 17,571	$
Novartis	14,670	21,775
Government contract	9,800	786
Other research collaborator	7,330	2,508
InterfeRx program, research reagent license and other	1,526	1,861
Total net revenues from research collaborators	$ 50,897	$ 26,930

Revenues increased significantly for the year ended December 31, 2007 as compared to the year ended December 31, 2006 primarily as a result of our August 2007 alliance with Roche. Under the Roche alliance, $278.2 million is being recognized as revenue on a straight-line basis over five years. In connection with the Roche alliance, Roche Kulmbach employees performed certain transition services for us at various levels through August 2008. We reimbursed Roche for these services at an agreed-upon rate. We recorded $4.2 million of these services as contra revenue (a reduction of revenues) during 2007.

The decrease in Novartis revenues during the year ended December 31, 2007 compared to the year ended December 31, 2006 was due to a decrease in the number of resources allocated to the broad Novartis alliance. The decrease in Novartis revenues was also due to a decrease in the number of resources allocated to, as well as lower external expense reimbursement under, our Novartis flu alliance, as a result of the shift in focus during 2007 on additional pre-clinical research prior to advancing the pandemic flu program into development. During 2008, the pandemic flu program was stopped and currently there are no specific resource commitments for this program.

For the year ended December 31, 2007, government contract revenues increased as a result of our collaboration with NIAID, which began in the fourth quarter of 2006, and our collaboration with DTRA, which began in the third quarter of 2007.

Other research collaborator revenues consisted primarily of research funding and amortization of upfront payments or license fees from Biogen Idec and Merck. The increase in other research collaborator revenues in 2007 was primarily the result of our collaboration with Biogen Idec, which began in the fourth quarter of 2006 and the

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termination of our Merck collaboration agreement in September 2007. We were recognizing the remaining deferred revenue under the Merck agreement on a straight-line basis over the remaining period of expected performance of four years. As a result of the termination, we recognized an aggregate of $3.5 million during the third quarter of 2007, which represented all of the remaining deferred revenue under the Merck agreement.

The decrease in InterfeRx program, research reagent license and other revenues for the year ended December 31, 2007 compared to the prior year was due to upfront payments pursuant to license agreements entered into under our InterfeRx program in the prior year.

Total deferred revenues of $263.3 million at December 31, 2007 consists of payments received from collaborators, primarily Roche, that we have yet to recognize pursuant to our revenue recognition policies.

Operating Expenses

The following tables summarize our operating expenses for the periods indicated, in thousands and as a percentage of total operating expenses, together with the changes, in thousands and percentages:

	2007	% of Total Operating Expenses	2006	% of Total Operating Expenses	Increase $	Increase %
Research and development	$ 120,686	84%	$ 49,260	74%	$ 71,426	145%
General and administrative	23,388	16%	17,171	26%	6,217	36%
Total operating expenses	$ 144,074	100%	$ 66,431	100%	$ 77,643	117%

Certain reclassifications have been made to prior years financial statements to conform to the 2007 presentation.

Research and development. The following table summarizes the components of our research and development expenses for the periods indicated, in thousands and as a percentage of total research and development expenses, together with the changes, in thousands and percentages:

	2007	% of Expense Category	2006	% of Expense Category	Increase $	Increase %
Research and development						
License fees	$ 42,207	35%	$ 4,040	8%	$ 38,167	945%
Clinical trial and manufacturing	20,662	17%	10,019	20%	10,643	106%
External services	18,417	15%	6,001	12%	12,416	207%
Compensation and related	13,201	11%	10,666	22%	2,535	24%
Non-cash stock-based compensation	9,363	8%	5,006	10%	4,357	87%
Facilities-related	8,511	7%	6,315	13%	2,196	35%
Lab supplies and materials	6,154	5%	5,462	11%	692	13%
Other	2,171	2%	1,751	4%	420	24%

Total research and development expenses	$ 120,686	100%	$ 49,260	100%	$ 71,426	145%

During the year ended December 31, 2007, our research and development expenses increased significantly compared to the year ended December 31, 2006 primarily as a result of an increase in license fees consisting of $27.5 million in payments to certain entities, primarily Isis, in connection with the Roche alliance and $14.7 million in charges for licenses for certain delivery technologies. The increase was also due to an increase in clinical trial and manufacturing expenses in support of our clinical program for RSV, for which we began Phase II trials in June 2007, as well as higher manufacturing expenses related to our pre-clinical development programs. The increase in external services was due to higher expenses related to our pre-clinical programs for the treatment of hypercholesterolemia, liver cancer and Ebola, as well as higher expenses associated with our delivery-related collaborations. The increase in compensation and related expenses and facilities-related expenses was due to additional research and development headcount over the past year to support our alliances and expanding product pipeline. The increase in non-cash stock-based compensation was due primarily to one-time charges of $2.9 million from restricted stock grants and stock option modifications in August 2007 relating to the transfer of our former German employees to Roche Kulmbach as part of our alliance with Roche.

General and administrative. The following table summarizes the components of our general and administrative expenses for the periods indicated, in thousands and as a percentage of total general and administrative expenses, together with the changes, in thousands and percentages:

	2007	% of Expense Category	2006	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
General and administrative						
Consulting and professional services	$ 8,547	36%	$ 5,162	30%	$ 3,385	66%
Non-cash stock-based compensation	5,109	22%	3,298	19%	1,811	55%
Compensation and related	4,647	20%	3,546	21%	1,101	31%
Facilities-related	2,486	11%	2,736	16%	(250)	(9)%
Insurance	654	3%	652	4%	2	0%
Other	1,945	8%	1,777	10%	168	9%
Total general and administrative expenses	$ 23,388	100%	$ 17,171	100%	$ 6,217	36%

The increase in general and administrative expenses in 2007 compared to the prior year was due primarily to professional service fees, which were the result of increased business development activities, including work related to our alliance with Roche and with Regulus Therapeutics, the company we formed with Isis to pursue microRNA-based therapeutics. The increase in compensation and related expenses was due primarily to an increase in headcount to support the overall corporate growth of the company. The increase in non-cash stock-based compensation was due primarily to one-time charges of $0.9 million from restricted stock grants and stock option modifications in August 2007 relating to the transfer of our former German employees to Roche Kulmbach as part of our alliance with Roche.

Other income (expense)

Interest income was $15.4 million in 2007 compared to $6.2 million in 2006. The increase was due to our higher average cash, cash equivalent and marketable securities balances, primarily from the $331.0 million in proceeds we received in August 2007 from our alliance with Roche.

Interest expense was $1.1 million in 2007 and $1.0 million in 2006. Interest expense in each year related to borrowings under our lines of credit used to finance capital equipment purchases.

Our provision for income taxes was $5.2 million in 2007 primarily as a result of the sale of our German operations to Roche in August 2007 for $15.0 million.

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Liquidity and Capital Resources

The following table summarizes our cash flow activities for the periods indicated, in thousands:

	Year Ended December 31, 2008	2007	2006
Net loss	$ (26,249)	$(85,466)	$ (34,608)
Adjustments to reconcile net loss to net cash used in operating activities	27,840	29,834	12,633
Changes in operating assets and liabilities	63,900	252,151	(2,655)
Net cash provided by (used in) operating activities	65,491	196,519	(24,630)
Net cash provided by (used in) investing activities	17,936	(277,425)	(30,046)
Net cash provided by financing activities	3,155	58,635	166,631
Effect of exchange rate on cash	53	(527)	243
Net increase (decrease) in cash and cash equivalents	86,635	(22,798)	112,198
Cash and cash equivalents, beginning of period	105,157	127,955	15,757
Cash and cash equivalents, end of period	$ 191,792	$105,157	$ 127,955

Since we commenced operations in 2002, we have generated significant losses. As of December 31, 2008, we had an accumulated deficit of $252.2 million. As of December 31, 2008, we had cash, cash equivalents and marketable securities of $512.7 million, compared to cash, cash equivalents and marketable securities of $455.6 million as of December 31, 2007. The increase in our cash, cash equivalents and marketable securities at December 31, 2008 was due primarily to our receipt of $120.0 million of upfront cash and technology transfer milestone payments under our Takeda alliance, partially offset by the funding of our operating expenses. We invest primarily in cash equivalents, U.S. government obligations, high-grade corporate notes and commercial paper. Our investment objectives are, primarily, to assure liquidity and preservation of capital and, secondarily, to obtain investment income. All of our investments in debt securities are recorded at fair value and are available-for-sale. Fair value is determined based on quoted market prices and models using observable data inputs. We have not recorded any impairment charges to our fixed income marketable securities as of December 31, 2008.

Operating activities

We have required significant amounts of cash to fund our operating activities as a result of net losses since our inception. The decrease in net cash provided by operating activities for the year ended December 31, 2008 compared to the year ended December 31, 2007 was due primarily to the proceeds received from our August 2007 Roche alliance, partially offset by the proceeds received from our May 2008 alliance with Takeda. Offsetting the proceeds from the Takeda alliance, the main components of our use of cash in operating activities for the year ended December 31, 2008 consisted of the net loss and changes in our working capital. Cash used in operating activities is adjusted for non-cash items to reconcile net loss to net cash provided by or used in operating activities. These non-cash adjustments consist primarily of stock-based compensation, equity in loss of joint venture and depreciation and amortization. We had an increase in deferred revenue of $66.7 million for the year ended December 31, 2008 due primarily to the proceeds received from our Takeda and Kyowa Hakko alliances.

We expect that we will require significant amounts of cash to fund our operating activities for the foreseeable future as we continue to develop and advance our research and development initiatives. The actual amount of overall expenditures will depend on numerous factors, including the timing of expenses, the timing and terms of collaboration agreements or other strategic transactions, if any, and the timing and progress of our research and development efforts.

Investing activities

For the year ended December 31, 2008, net cash provided by investing activities resulted primarily from net sales and maturities of marketable securities of $28.8 million. Also included in our investing activities for the year ended December 31, 2008 were purchases of property and equipment of $10.8 million related to the expansion of our Cambridge facility. For the year ended December 31, 2007, net cash used in investing activities of $277.4 million resulted primarily from purchases of marketable securities of $544.4 million due primarily to the investments made with the proceeds from the Roche alliance, partially offset by sales and maturities of marketable securities of $283.3 million. Also included in our investing activities for the year ended December 31, 2007 was a $10.0 million cash contribution made to Regulus Therapeutics in connection with its formation, as well as purchases of property and equipment of $7.8 million related to the expansion of our Cambridge facility.

Financing activities

For the year ended December 31, 2008, net cash provided by financing activities was $3.2 million as compared to $58.6 million provided by financing activities for the year ended December 31, 2007. For the year ended December 31, 2008, net cash provided by financing activities was due primarily to proceeds of $5.4 million from our issuance of shares to Novartis in May 2008. Net cash provided by financing activities for the year ended December 31, 2007 consisted primarily of proceeds of $42.5 million from our sale of 1,975,000 shares of our common stock to Roche in connection with the establishment of the Roche alliance.

In March 2006, we entered into an agreement with Oxford to establish an equipment line of credit for up to $7.0 million to help support capital expansion of our facility in Cambridge, Massachusetts and capital equipment purchases. During 2006, we borrowed an aggregate of $4.2 million from Oxford pursuant to the agreement. In May 2007, we borrowed an aggregate of $1.0 million from Oxford pursuant to the agreement. In March 2004, we entered into an equipment line of credit with Lighthouse to finance leasehold improvements and equipment purchases of up to $10.0 million. On the maturity of each equipment advance under the Lighthouse line of credit, we were required to pay, in addition to the principal and interest due, an additional amount of 11.5% of the original principal. This amount was being accrued over the applicable borrowing period as additional interest expense. In December 2008, we defeased the aggregate outstanding balance under the Oxford and Lighthouse credit lines.

During the current downturn in global financial markets, some companies have experienced difficulties accessing their cash equivalents, investment securities and raising capital generally, which have had a material adverse impact on their liquidity. In addition, the current economic downturn has severely diminished the availability of capital and may limit our ability to access these markets to obtain financing in the future. Based on our current operating plan, we believe that our existing cash, cash equivalents and fixed income marketable securities, for which we have not recognized any impairment charges, together with the cash we expect to generate under our current alliances, including our Novartis, Roche and Takeda alliances, will be sufficient to fund our planned operations for at least the next several years, during which time we expect to further the development of our product candidates, conduct clinical trials, extend the capabilities of our technology platform and continue to prosecute patent applications and otherwise build and maintain our patent portfolio. However, we may require significant additional funds earlier than we currently expect in order to develop, commence clinical trials for and commercialize any product candidates.

In the longer term, we may seek additional funding through additional collaborative arrangements and public or private financings. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our existing stockholders may result. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue.

Even if we are able to raise additional funds in a timely manner, our future capital requirements may vary from what we expect and will depend on many factors, including:

- our progress in demonstrating that siRNAs can be active as drugs;

our ability to develop relatively standard procedures for selecting and modifying siRNA drug candidates;

progress in our research and development programs, as well as the magnitude of these programs;

the timing, receipt and amount of milestone and other payments, if any, from present and future collaborators, if any;

the timing, receipt and amount of funding under current and future government contracts, if any;

our ability to maintain and establish additional collaborative arrangements;

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the resources, time and costs required to successfully initiate and complete our pre-clinical and clinical trials, obtain regulatory approvals, protect our intellectual property and obtain and maintain licenses to third-party intellectual property;

the cost of preparing, filing, prosecuting, maintaining and enforcing patent claims;

progress in the research and development programs of Regulus Therapeutics; and

the timing, receipt and amount of sales and royalties, if any, from our potential products.

Off-Balance Sheet Arrangements

In connection with a certain license agreement, we are required to indemnify the licensor for certain damages arising in connection with the intellectual property rights licensed under the agreement. In addition, we are a party to a number of agreements entered into in the ordinary course of business, which contain typical provisions, which obligate us to indemnify the other parties to such agreements upon the occurrence of certain events. These indemnification obligations are considered off-balance sheet arrangements in accordance with FASB Interpretation No. 45, Guarantor s Accounting and Disclosure Requirements for Guarantees, Including Indirect Guarantees of Indebtedness of Others. To date, we have not encountered material costs as a result of such obligations and have not accrued any liabilities related to such obligations and have not accrued any liabilities related to such obligations in our financial statements. See Note 7 to our consolidated financial statements included in this annual report on Form 10-K for further discussion of these indemnification agreements.

Contractual Obligations

In the table below, we set forth our enforceable and legally binding obligations and future commitments as of December 31, 2008, as well as obligations related to contracts that we are likely to continue, regardless of the fact that they were cancelable as of December 31, 2008. Some of the figures that we include in this table are based on management s estimate and assumptions about these obligations, including their duration, the possibility of renewal, anticipated actions by third parties, and other factors. Because these estimates and assumptions are necessarily subjective, the obligations we will actually pay in future periods may vary from those reflected in the table.

	Payments Due by Period				
Contractual Obligations	**2009**	**2010 and 2011**	**2012 and 2013**	**After 2013**	**Total**
Operating lease obligations(1)	$ 3,296	$ 5,768	$	$	$ 9,064
Purchase commitments(2)	8,721	523			9,244
Technology-related commitments(3)	3,612	5,091	1,922	5,700	16,325
Total contractual cash obligations	$ 15,629	$ 11,382	$ 1,922	$ 5,700	$ 34,633

(1) Relates to our Cambridge, Massachusetts non-cancelable operating lease agreements.

(2) Includes commitments related to non-cancelable purchase orders, clinical and pre-clinical agreements and other significant purchase commitments for good or services. Amounts have not been adjusted to reflect our January 2009 agreement with Cubist, under which Cubist will bear one-half of the development costs related to our ALN-RSV program.

(3) Relates to our fixed payment obligations under license agreements, as well as other payments related to technology research and development. Does not include license fees due to certain of our licensors in accordance with the applicable license agreements with those parties as a result of our January 2009 agreement with Cubist.

We in-license technology from a number of sources. Pursuant to these in-license agreements, we will be required to make additional payments if and when we achieve specified development and regulatory milestones. To the extent we are unable to reasonably predict the likelihood, timing or amount of such payments, we have excluded them from the table above.

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Recent Accounting Pronouncements

Effective January 1, 2008, we implemented SFAS No. 157, Fair Value Measurements, or SFAS 157. SFAS 157 clarifies the principle that fair value should be based on the assumptions market participants would use when pricing an asset or liability and establishes a fair value hierarchy that prioritizes the information used to develop those assumptions. Under the standard, fair value measurements would be separately disclosed by level within the fair value hierarchy. Our partial adoption of SFAS 157 has had no impact on our operating results or financial position. We are evaluating the impact, if any, full adoption of SFAS 157 will have on our nonfinancial assets and liabilities within the scope of SFAS 157.

In December 2007, the FASB reached a consensus on EITF Issue No. 07-1, Accounting for Collaborative Arrangements, or EITF 07-1. EITF 07-1 requires collaborators to present the results of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational and consistently applied accounting policy election. Further, EITF 07-1 clarifies that the determination of whether transactions within a collaborative arrangement are part of a vendor-customer (or analogous) relationship subject to EITF 01-9. EITF 07-1 became effective on January 1, 2009. We are evaluating the potential impact of EITF 07-1 on our consolidated financial statements.

In December 2007, the FASB issued SFAS No. 141R, Business Combinations, or SFAS 141R. SFAS 141R establishes principles and requirements for how an acquirer recognizes and measures in its financial statements the identifiable assets acquired, the liabilities assumed, any noncontrolling interest in the acquiree and the goodwill acquired. SFAS 141R also establishes disclosure requirements to enable the evaluation of the nature and financial effects of the business combination. SFAS 141R is effective for fiscal year 2009 and is not expected to have a material impact on our consolidated financial statements.

In December 2007, the FASB issued SFAS No. 160, Noncontrolling Interests in Consolidated Financial Statements, an amendment of ARB No. 51, or SFAS 160. SFAS 160 changes the accounting for and reporting of noncontrolling or minority interests (now called noncontrolling interests) in consolidated financial statements. SFAS 160 become effective on January 1, 2009. When implemented, prior periods will be recast for the changes required by SFAS 160. We do not anticipate the adoption of SFAS 160 will have a material impact on our consolidated financial statements.

In May 2008, the FASB issued SFAS No. 162, The Hierarchy of Generally Accepted Accounting Principles, or SFAS 162. SFAS 162 identifies the sources of accounting principles and the framework for selecting the principles used (order of authority) in the preparation of financial statements that are presented in conformity with generally accepted accounting standards in the United States. The adoption of SFAS 162 did not have a material impact on our consolidated financial statements.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As part of our investment portfolio, we own financial instruments that are sensitive to market risks. The investment portfolio is used to preserve our capital until it is required to fund operations, including our research and development activities. Our marketable securities consist of U.S. government obligations, high-grade corporate notes and commercial paper. All of our investments in debt securities are classified as available-for-sale and are recorded at fair value. Our available-for-sale investments in debt securities are sensitive to changes in interest rates and changes in the credit ratings of the issuers. Interest rate changes would result in a change in the net fair value of these financial instruments due to the difference between the market interest rate and the market interest rate at the date of purchase of the financial instrument. A 10% decrease in market interest rates at December 31, 2008 would impact the net fair value of such interest-sensitive financial instruments by $1.8 million. A downgrade in the credit rating of an issuer of a debt security or further deterioration of the credit markets could result in a decline in the fair value of the debt instruments. Our investment guidelines prohibit investment in auction rate securities and we do not believe we have any direct exposure to losses relating from mortgage-based securities or derivatives related thereto such as credit-default swaps. We have not recorded any impairment charges to our fixed income marketable securities as of December 31, 2008.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

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Management s Annual Report on Internal Control Over Financial Reporting

The management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Securities Exchange Act of 1934 as a process designed by, or under the supervision of, the company s principal executive and principal financial officers and effected by the company s board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of the assets of the Company;

Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only in accordance with authorizations of management and directors of the Company; and

Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company s assets that could have a material effect on the financial statements.

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

The Company s management assessed the effectiveness of the Company s internal control over financial reporting as of December 31, 2008. In making this assessment, the Company s management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework.

Based on our assessment, management concluded that, as of December 31, 2008, the Company s internal control over financial reporting is effective based on those criteria.

The effectiveness of the Company s internal control over financial reporting as of December 31, 2008 has been audited by PricewaterhouseCoopers LLP, an independent registered public accounting firm, as stated in their report. This report appears on page 89.

Report of Independent Registered Public Accounting Firm

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

In our opinion, based on our audits and the report of other auditors, the accompanying consolidated balance sheets and the related consolidated statements of operations and comprehensive loss, stockholders equity and cash flows present fairly, in all material respects, the financial position of Alnylam Pharmaceuticals, Inc. and its subsidiaries at December 31, 2008 and 2007, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2008 in conformity with accounting principles generally accepted in the United States of America. Also in our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2008, based on criteria established in *Internal Control Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). The Company s management is responsible for these financial statements, for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in Management s Annual Report on Internal Control over Financial Reporting. Our responsibility is to express opinions on these financial statements and on the Company s internal control over financial reporting based on our integrated audits. We did not audit the financial statements of Regulus Therapeutics LLC, an approximate 49 percent-owned equity investment, which were audited by other auditors whose report thereon has been furnished to us. Our opinion expressed herein, insofar as it relates to the Company s net investment in (approximately $1.6 million and $9.1 million at December 31, 2008 and 2007, respectively) and equity in the net loss (approximately $9.3 million and $1.1 million for the year ended December 31, 2008 and for the period from September 6, 2007 (inception) to December 31, 2007, respectively) of Regulus Therapeutics LLC, is based solely on the report of the other auditors. We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement and whether effective internal control over financial reporting was maintained in all material respects. Our audits of the financial statements included examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. Our audit of internal control over financial reporting included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk. Our audits also included performing such other procedures as we considered necessary in the circumstances. We believe that our audits and the report of other auditors provide a reasonable basis for our opinions.

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

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

/s/ PricewaterhouseCoopers LLP

Boston, Massachusetts
March 2, 2009

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ALNYLAM PHARMACEUTICALS, INC.

CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)

	December 31, 2008	December 31, 2007
ASSETS		
Current assets:		
Cash and cash equivalents	$ 191,792	$ 105,157
Marketable securities	238,596	284,791
Collaboration receivables	4,188	5,031
Prepaid expenses and other current assets	4,674	2,926
Restricted cash	2,999	
Total current assets	442,249	397,905
Marketable securities	82,321	65,654
Property and equipment, net	19,194	13,810
Deferred tax assets	5,382	
Investment in joint venture (Regulus Therapeutics LLC)	1,583	9,129
Intangible assets, net	795	968
Restricted cash, net of current portion	3,152	6,152
Other assets		173
Total assets	$ 554,676	$ 493,791
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 2,588	$ 3,826
Accrued expenses	9,328	11,724
Income taxes payable	6,111	3,497
Current portion of notes payable		3,795
Deferred rent	1,561	1,387
Deferred revenue	79,864	59,249
Total current liabilities	99,452	83,478
Deferred rent, net of current portion	2,732	3,813
Deferred revenue, net of current portion	250,121	204,067
Notes payable, net of current portion		2,963
Other long-term liabilities	246	302
Total liabilities	352,551	294,623
Commitments and contingencies (Notes 7 and 12)		
Stockholders equity:		

Preferred stock, $0.01 par value, 5,000,000 shares authorized and no shares issued and outstanding at December 31, 2008 and 2007		
Common stock, $0.01 par value, 125,000,000 shares authorized; 41,413,828 shares issued and outstanding at December 31, 2008; 40,772,967 shares issued and outstanding at December 31, 2007	414	408
Additional paid-in capital	452,767	424,453
Accumulated other comprehensive income	1,186	300
Accumulated deficit	(252,242)	(225,993)
Total stockholders equity	202,125	199,168
Total liabilities and stockholders equity	$ 554,676	$ 493,791

The accompanying notes are an integral part of these consolidated financial statements.

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ALNYLAM PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except per share amounts)

	Year Ended December 31, 2008	2007	2006
Net revenues from research collaborators	$ 96,163	$ 50,897	$ 26,930
Operating expenses:			
Research and development(1)	96,883	120,686	49,260
General and administrative(1)	27,115	23,388	17,171
Total operating expenses	123,998	144,074	66,431
Loss from operations	(27,835)	(93,177)	(39,501)
Other income (expense):			
Equity in loss of joint venture (Regulus Therapeutics LLC)	(9,290)	(1,075)	
Interest income	14,414	15,393	6,177
Interest expense	(872)	(1,083)	(1,029)
Other expense	(1,947)	(279)	(255)
Total other income (expense)	2,305	12,956	4,893
Loss before income taxes	(25,530)	(80,221)	(34,608)
Provision for income taxes	(719)	(5,245)	
Net loss	$ (26,249)	$ (85,466)	$ (34,608)
Net loss per common share basic and diluted	$ (0.64)	$ (2.21)	$ (1.09)
Weighted average common shares used to compute basic and diluted net loss per common share	41,077	38,657	31,890
Comprehensive loss:			
Net loss	$ (26,249)	$ (85,466)	$ (34,608)
Foreign currency translation	53	(598)	665
Unrealized gain on marketable securities	833	258	117
Comprehensive loss	$ (25,363)	$ (85,806)	$ (33,826)

(1) Non-cash stock-based compensation expenses included in operating expenses are as follows:

Research and development	$ 9,575	$ 9,363	$ 5,006
General and administrative	6,807	5,109	3,298

The accompanying notes are an integral part of these consolidated financial statements.

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ALNYLAM PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS EQUITY
(In thousands, except share amounts)

	Common Stock		Additional Paid-in	Deferred Stock-based	Accumulated Other Comprehensive (Loss)	Accumulated	Total Stockholders
	Shares	Amount	Capital	Compensation	Income	Deficit	Equity
Balance at December 31, 2005	26,638,255	$ 267	$ 170,033	$ (2,460)	$ (142)	$ (105,919)	$ 61,779
Exercise of common stock options and warrants	539,425	5	998				1,003
Issuance of common stock	56,990	1	591				592
Deferred compensation related to stock options and restricted stock			1,614	(467)			1,147
Amortization of deferred compensation expense related to stock options and restricted stock			4,318	2,838			7,156
Issuance of common stock upon public offerings, net of offering costs of $6,586	9,815,961	98	163,225				163,323
Foreign currency translation					665		665
Unrealized gain on marketable securities					117		117
Net loss						(34,608)	(34,608)
Balance at December 31, 2006	37,050,631	371	340,779	(89)	640	(140,527)	201,174
	1,247,808	12	9,232				9,244

Exercise of common stock options							
Issuance of common stock	2,474,528	25	59,874				59,899
Stock-based compensation expense			14,364	89			14,453
Foreign currency translation					(598)		(598)
Joint venture stock compensation (Regulus Therapeutics LLC)			204				204
Unrealized gain on marketable securities					258		258
Net loss						(85,466)	(85,466)
Balance at December 31, 2007	40,772,967	408	424,453		300	(225,993)	199,168
Exercise of common stock options	377,228	4	3,782				3,786
Issuance of common stock	263,633	2	6,507				6,509
Stock-based compensation expense			16,381				16,381
Foreign currency translation					53		53
Joint venture stock compensation (Regulus Therapeutics LLC)			1,644				1,644
Unrealized gain on marketable securities					833		833
Net loss						(26,249)	(26,249)
Balance at December 31, 2008	41,413,828	$ 414	$ 452,767	$	$ 1,186	$ (252,242)	$ 202,125

The accompanying notes are an integral part of these consolidated financial statements.

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ALNYLAM PHARMACEUTICALS, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31, 2008	2007	2006
Cash flows from operating activities:			
Net loss	$ (26,249)	$ (85,466)	$ (34,608)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Depreciation and amortization	5,726	4,082	4,070
Deferred income tax (benefit) provision	(5,501)	1,889	
Non-cash stock-based compensation	18,026	14,676	8,304
Non-cash license expense		7,909	130
Charge for 401(k) company stock match	382	407	129
Equity in loss of joint venture (Regulus Therapeutics LLC)	7,646	871	
Impairment on equity investment	1,561		
Changes in operating assets and liabilities:			
Proceeds from landlord tenant improvements	581	2,621	1,106
Collaboration receivables	843	(1,194)	(3,220)
Prepaid expenses and other assets	(1,748)	(4,348)	(336)
Accounts payable	(1,238)	(264)	2,088
Income taxes payable	2,614	3,497	
Accrued expenses and other	(3,821)	6,843	611
Deferred revenue	66,669	244,996	(2,904)
Net cash provided by (used in) operating activities	65,491	196,519	(24,630)
Cash flows from investing activities:			
Purchases of property and equipment	(10,764)	(7,788)	(4,986)
Disposals of property and equipment		2,342	
Increase in restricted cash		(839)	
Purchases of marketable securities	(482,244)	(544,394)	(172,303)
Sales and maturities of marketable securities	511,044	283,254	147,243
Investment in joint venture (Regulus Therapeutics LLC)	(100)	(10,000)	
Net cash provided by (used in) investing activities	17,936	(277,425)	(30,046)
Cash flows from financing activities:			
Proceeds from issuance of common stock, net of issuance costs	4,505	61,011	164,890
Proceeds from issuance of shares to Novartis	5,408		
Proceeds from notes payable		957	4,000
Repayments of notes payable	(6,758)	(3,333)	(2,259)
Net cash provided by financing activities	3,155	58,635	166,631

Effect of exchange rate on cash		53		(527)		243
Net increase (decrease) in cash and cash equivalents		86,635		(22,798)		112,198
Cash and cash equivalents, beginning of period		105,157		127,955		15,757
Cash and cash equivalents, end of period	$	191,792	$	105,157	$	127,955
Supplemental disclosure of cash flows						
Cash paid for interest	$	1,499	$	890	$	726
Cash paid for income taxes	$	2,671	$		$	
Supplemental disclosure of non-cash financing activities						
Common stock issued in connection with license agreements	$		$	7,909	$	130

The accompanying notes are an integral part of these consolidated financial statements.

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ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. NATURE OF BUSINESS

Alnylam Pharmaceuticals, Inc. (the Company or Alnylam) commenced operations on June 14, 2002 as a biopharmaceutical company seeking to develop and commercialize novel therapeutics based on RNA interference (RNAi). Alnylam is focused on discovering, developing and commercializing RNAi therapeutics by establishing strategic alliances with leading pharmaceutical and biotechnology companies, establishing and maintaining a strong intellectual property position in the RNAi field, generating revenues through licensing agreements and ultimately developing and commercializing RNAi therapeutics for its own account. The Company has devoted substantially all of its efforts to business planning, research and development, acquiring, filing and expanding intellectual property rights, recruiting management and technical staff, and raising capital.

2. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Principles of Consolidation

The Company comprises four entities, Alnylam Pharmaceuticals, Inc. (the parent company) and three wholly-owned subsidiaries (Alnylam U.S., Inc., Alnylam Europe AG (Alnylam Europe) and Alnylam Securities Corporation). Alnylam Pharmaceuticals, Inc. is a Delaware corporation that was formed on May 8, 2003. Alnylam U.S., Inc. is also a Delaware corporation that was formed on June 14, 2002. Alnylam Securities Corporation is a Massachusetts corporation that was formed on December 19, 2006. Alnylam Europe was incorporated in Germany in June 2000 under the name Ribopharma AG. The Company acquired Alnylam Europe in July 2003.

The accompanying consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiaries. All significant intercompany accounts and transactions have been eliminated. The Company uses the equity method of accounting to account for its investment in Regulus Therapeutics LLC (Regulus Therapeutics).

Reclassifications

Certain reclassifications have been made to prior years financial statements to conform to the 2008 presentation.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Concentrations of Credit Risk and Significant Customers

Financial instruments which potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and marketable securities. As of December 31, 2008 and 2007, substantially all of the Company s cash, cash equivalents and marketable securities were invested in money market mutual funds, commercial paper, corporate notes and government securities through highly rated financial institutions.

To date, the Company s revenues from collaborations have been generated from primarily F. Hoffmann-La Roche Ltd and certain of its affiliates (collectively, Roche), Novartis Pharma AG and one of its affiliates (collectively, Novartis) and Takeda Pharmaceutical Company Limited (Takeda). Novartis owned approximately 13.2% of the Company s outstanding common stock as of December 31, 2008. In 2008, the Company had revenue from Roche, Takeda and Novartis, which accounted for 57%, 13% and 12%, respectively, of

ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

the Company s total revenue. In 2007, the Company had revenue from Roche, Novartis and the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), which accounted for 35%, 29% and 15%, respectively, of the Company s total revenue. In 2006, the Company had revenue from Novartis, which accounted for 81% of the Company s total revenue. Receivables from Novartis, NIAID and the Defense Threat Reduction Agency (DTRA), an agency of the United States Department of Defense, represented approximately 55%, 22% and 10%, respectively, of the Company s collaboration receivables balance at December 31, 2008. Receivables from Novartis, NIAID and DTRA represented approximately 43%, 36% and 15%, respectively, of the Company s collaboration receivables balance at December 31, 2007.

Fair Value Measurements

Effective January 1, 2008, the Company implemented Statement of Financial Accounting Standards (SFAS) No. 157, *Fair Value Measurements* (SFAS 157), which addresses how companies should measure fair value when they are required to do so for recognition or disclosure purposes. The standard provides a common definition of fair value and is intended to make the measurement of fair value more consistent and comparable as well as to improve disclosures about those measures. This standard formalizes the measurement principles to be utilized in determining fair value for purposes such as derivative valuation and impairment analysis. The partial adoption of SFAS 157 by the Company has had no impact on the Company s operating results or financial position. The Company is evaluating the impact, if any, full adoption of this standard will have on its non-financial assets and liabilities within the scope of SFAS 157. For recognition purposes, on a recurring basis, the Company is required to measure certain cash equivalents and available-for-sale investments at fair value. Changes in the fair value of these investments historically have been insignificant.

The following table presents information about the Company s assets that are measured at fair value on a recurring basis as of December 31, 2008, and indicates the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value. In general, fair values determined by Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities. Fair values determined by Level 2 inputs utilize data points that are observable, such as quoted prices (adjusted), interest rates and yield curves. Fair values determined by Level 3 inputs utilize unobservable data points for the asset or liability, and include situations where there is little, if any, market activity for the asset or liability. Financial assets and liabilities measured at fair value on a recurring basis are summarized as follows, in thousands:

Description	**As of December 31, 2008**	**Quoted Prices in Active Markets (Level 1)**	**Significant Observable Inputs (Level 2)**	**Significant Unobservable Inputs (Level 3)**
Cash equivalents	$ 187,057	$ 167,293	$ 19,764	$
Marketable securities (fixed income)	320,269		320,269	
Marketable securities (equity holdings)	648		648	
Total	$ 507,974	$ 167,293	$ 340,681	$

The carrying amounts reflected in the Company s consolidated balance sheets for cash, collaboration receivables, other current assets, accounts payable and accrued expenses approximate fair value due to their short-term maturities.

The Company adopted the provisions of SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities* (SFAS 159), effective January 1, 2008. SFAS 159 allows an entity the irrevocable option to elect fair value for the initial and subsequent measurement for certain financial assets and liabilities on a contract-by-contract basis. The Company has not elected the fair value option for any of its financial assets or liabilities in the year ended December 31, 2008.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Investments in Marketable Securities

The Company invests its excess cash balances in short-term and long-term marketable debt and equity securities. The Company accounts for its investments in debt and equity securities under SFAS No. 115, *Accounting for Certain Investments in Debt and Equity Securities.* The Company classifies its investments in marketable debt securities as either held-to-maturity or available-for-sale based on facts and circumstances present at the time it purchased the securities. As of each balance sheet date presented, the Company classified all of its investments in debt securities as available-for-sale. The Company reports available-for-sale investments at fair value as of each balance sheet date and includes any unrealized holding gains and losses (the adjustment to fair value) in stockholders equity. Realized gains and losses are determined using the specific identification method and are included in investment income. If any adjustment to fair value reflects a decline in the value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is other than temporary and, if so, marks the investment to market through a charge to its consolidated statement of operations. The Company did not record any impairment charges related to its fixed income marketable securities during the years ended December 31, 2008, 2007 or 2006. During 2008, the Company recorded an impairment charge of $1.6 million related to its equity investment in Tekmira Pharmaceuticals Corporation (Tekmira), as the decrease in the fair value of this investment was deemed to be other than temporary. The Company s marketable securities are classified as cash equivalents if the original maturity, from the date of purchase, is 90 days or less, and as marketable securities if the original maturity, from the date of purchase, is in excess of 90 days.

The following tables summarize the Company s marketable securities at December 31, 2008 and 2007, in thousands:

	December 31, 2008			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper (Due within 1 year)	$ 56,014	$ 119	$	$ 56,133
Corporate notes (Due within 1 year)	37,504	262	(102)	37,664
Corporate notes (Due after 1 year through 2 years)	30,497	81	(106)	30,472
U.S. Government obligations (Due within 1 year)	143,872	927		144,799
U.S. Government obligations (Due after 1 year through 2 years)	50,649	552		51,201
Equity securities	1,345		(697)	648
Total	$ 319,881	$ 1,941	$ (905)	$ 320,917

	December 31, 2007			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value

Commercial paper (Due within 1 year)	$ 210,213	$ 177	$ (1)	$ 210,389
Municipal notes (Due within 1 year)	61,605			61,605
Municipal notes (Due after 1 year through 2 years)	7,340	12		7,352
Corporate notes (Due within 1 year)	6,452		(12)	6,440
Corporate notes (Due after 1 year through 2 years)	37,345	108	(41)	37,412
U.S. Government obligations (Due after 1 year through 2 years)	27,193	54		27,247
Total	$ 350,148	$ 351	$ (54)	$ 350,445

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Revenue Recognition

The Company has entered into collaboration agreements with biotechnology and pharmaceutical companies, including Roche, Takeda, Novartis, Kyowa Hakko Kirin Co., Ltd. (Kyowa Hakko), Biogen Idec Inc. (Biogen Idec) and Merck & Co., Inc. (Merck). The terms of the Company s collaboration agreements typically include non-refundable license fees, funding of research and development, payments based upon achievement of clinical and pre-clinical development milestones and royalties on product sales. The Company follows the provisions of the Securities and Exchange Commission s (SEC) Staff Accounting Bulletin (SAB) No. 104, *Revenue Recognition in Financial Statements,* Emerging Issues Task Force (EITF) Issue No. 00-21, *Revenue Arrangements with Multiple Deliverables* (EITF 00-21), EITF Issue No. 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent,* and EITF 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).

Non-refundable license fees are recognized as revenue upon delivery of the license only if the Company has a contractual right to receive such payment, the contract price is fixed or determinable, the collection of the resulting receivable is reasonably assured and the Company has no further performance obligations under the license agreement. Multiple element arrangements, such as license and development arrangements, are analyzed to determine whether the deliverables, which often include a license and performance obligations such as research and steering committee services, can be separated or whether they must be accounted for as a single unit of accounting in accordance with EITF 00-21. The Company recognizes up-front license payments as revenue upon delivery of the license only if the license has stand-alone value and the fair value of the undelivered performance obligations, typically including research and/or steering committee services, can be determined. If the fair value of the undelivered performance obligations can be determined, such obligations are accounted for separately as such obligations are fulfilled. If the license is considered to either not have stand-alone value or have stand-alone value but the fair value of any of the undelivered performance obligations cannot be determined, the arrangement would then be accounted for as a single unit of accounting and the license payments and payments for performance obligations are recognized as revenue over the estimated period of when the performance obligations are performed.

Whenever the Company determines that an arrangement should be accounted for as a single unit of accounting, the Company determines the period over which the performance obligations will be performed and revenue will be recognized. Revenue will be recognized using either a proportional performance or straight-line method. The Company recognizes revenue using the proportional performance method when the level of effort required to complete its performance obligations under an arrangement can be reasonably estimated and such performance obligations are provided on a best-efforts basis. Direct labor hours or full-time equivalents are typically used as the measure of performance. Revenue recognized under the proportional performance method would be determined by multiplying the total payments under the contract, excluding royalties and payments contingent upon achievement of substantive milestones, by the ratio of level of effort incurred to date to estimated total level of effort required to complete the Company s performance obligations under the arrangement. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the proportional performance method, as of the period ending date.

If the level of effort to complete its performance obligations under an arrangement cannot be reasonably estimated, then revenue under the arrangement would be recognized as revenue on a straight-line basis over the period the Company is expected to complete its performance obligations. Revenue is limited to the lesser of the cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the straight-line method, as of the period ending date.

Many of the Company s collaboration agreements entitle it to additional payments upon the achievement of performance-based milestones. If the achievement of a milestone is considered probable at the inception of the collaboration, the related milestone payment is included with other collaboration consideration, such as up-front fees and research funding, in the Company s revenue model. Milestones that involve substantial effort on the Company s part and the achievement of which are not considered probable at the inception of the collaboration are

ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

considered substantive milestones. Substantive milestones are included in the Company s revenue model when achievement of the milestone is considered probable. As future substantive milestones are achieved, a portion of the milestone payment, equal to the percentage of the performance period completed when the milestone is achieved, multiplied by the amount of the milestone payment, will be recognized as revenue upon achievement of such milestone. The remaining portion of the milestone will be recognized over the remaining performance period using the proportional performance or straight-line method. Milestones that are tied to regulatory approval are not considered probable of being achieved until such approval is received. Milestones tied to counter-party performance are not included in the Company s revenue model until the performance conditions are met.

Steering committee services that are not inconsequential or perfunctory and that are determined to be performance obligations are combined with other research services or performance obligations required under an arrangement, if any, in determining the level of effort required in an arrangement and the period over which the Company expects to complete its aggregate performance obligations.

For revenue generating arrangements where the Company, as a vendor, provides consideration to a licensor or collaborator, as a customer, the Company applies the provisions of EITF 01-9. EITF 01-9 addresses the accounting for revenue arrangements where both the vendor and the customer make cash payments to each other for services and/or products. A payment to a customer is presumed to be a reduction of the selling price unless the Company receives an identifiable benefit for the payment and it can reasonably estimate the fair value of the benefit received. Payments to a customer that are deemed a reduction of selling price are recorded first as a reduction of revenue, to the extent of both cumulative revenue recorded to date and probable future revenues, which include any unamortized deferred revenue balances, under all arrangements with such customer, and then as an expense. Payments that are not deemed to be a reduction of selling price would be recorded as an expense.

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying consolidated balance sheets. Amounts not expected to be recognized within the next 12 months are classified as long-term deferred revenue. As of December 31, 2008, the Company had short-term and long-term deferred revenue of $79.9 million and $250.1 million, respectively, related to its collaborations.

Income Taxes

The Company uses the asset and liability method of accounting for income taxes. Under the asset and liability method, deferred tax assets and liabilities reflect the impact of temporary differences between amounts of assets and liabilities for financial reporting purposes and such amounts as measured under enacted tax laws. A valuation allowance is required to offset any net deferred tax assets if, based upon the available evidence, it is more likely than not that some or all of the deferred tax asset will not be realized.

Research and Development Costs

Research and development costs are expensed as incurred. Included in research and development costs are wages, benefits and other operating costs, facilities, supplies, external services, clinical trial and manufacturing costs and overhead directly related to the Company s research and development department as well as costs to acquire technology licenses.

The Company has entered into several license agreements for rights to utilize certain technologies. The terms of the licenses may provide for upfront payments, annual maintenance payments, milestone payments based upon certain specified events being achieved and royalties on product sales. Costs to acquire and maintain licensed technology that has not reached technological feasibility and does not have alternative future use are charged to research and development expense as incurred. During the years ended December 31, 2008, 2007 and 2006, the Company charged to research and development expense $12.6 million, $42.2 million and $4.0 million, respectively, of costs associated with license fees. License fees for 2007 were primarily the result of $27.5 million in payments to

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

certain entities, primarily Isis Pharmaceuticals, Inc. (Isis), in connection with the Roche alliance and $14.7 million in charges for licenses for certain delivery technologies.

Accounting for Stock-Based Compensation

Effective January 1, 2006, the Company adopted the fair value recognition provisions of SFAS No. 123R, *Share-Based Payment, an amendment of FASB Statements Nos. 123 and 95* (SFAS 123R), using the modified-prospective-transition method. The Company has stock option plans and an employee stock purchase plan under which it grants equity instruments that are required to be evaluated under SFAS 123R. For stock options granted to non-employees, the Company recognizes compensation expense in accordance with the requirements of SFAS No. 123, *Accounting for Stock-Based Compensation* (SFAS 123) and EITF Issue No. 96-18, *Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services* under which compensation expense is generally recognized over the vesting period of the award, which is generally the period during which services are rendered by such non-employees. At the end of each financial reporting period prior to vesting, the value of these options (as calculated using the Black-Scholes option-pricing model) is re-measured using the then-current fair value of the Company s common stock. Stock options granted by the Company to non-employees, other than members of the Company s Board of Directors, generally vest over a four-year service period. The Company accounts for non-employee grants as an expense over the vesting period of the underlying stock options using the method prescribed by Financial Accounting Standards Board (FASB) Interpretation No. 28, *Accounting for Stock Appreciation Rights and Other Variable Stock Option or Award Plans an interpretation of APB Opinions No. 15 and 25* (FIN 28).

Foreign Currency

The Company s foreign subsidiary, Alnylam Europe (a German-based company), has designated its local currency, the Euro, as its functional currency. Financial statements of this foreign subsidiary are translated to United States dollars for consolidation purposes using current rates of exchange for assets and liabilities; equity is translated using historical exchange rates; and revenue and expense amounts are translated using the average exchange rate for the period. Net unrealized gains and losses resulting from foreign currency translation are included in other comprehensive income (loss) which is a separate component of stockholders equity. Net realized gains and losses from foreign currency transactions are included in the consolidated statements of operations. The Company recognized a loss of $0.4 million during 2008, a gain of $0.1 million during 2007 and a loss of $0.3 million during 2006 from foreign currency transactions.

Comprehensive Loss

Comprehensive loss is comprised of net loss and certain changes in stockholders equity that are excluded from net loss. The Company includes foreign currency translation adjustments in other comprehensive loss for Alnylam Europe as the functional currency is not the United States dollar. The Company also includes unrealized gains and losses on certain marketable securities in other comprehensive loss.

Net Loss Per Common Share

The Company accounts for and discloses net loss per common share in accordance with SFAS No. 128, *Earnings per Share*. Basic net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding. Diluted net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares and dilutive potential common share equivalents then outstanding. Potential common shares consist of shares issuable upon the exercise of stock options (using the treasury stock method), and unvested restricted stock awards. Because the inclusion of potential common shares would be anti-dilutive for all periods presented, diluted net loss per common share is the same as basic net loss per common share.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The following table sets forth for the periods presented the potential common shares (prior to consideration of the treasury stock method) excluded from the calculation of net loss per common share because their inclusion would be anti-dilutive, in thousands:

	December 31,		
	2008	**2007**	**2006**
Options to purchase common stock	7,037	5,304	4,650
Unvested restricted common stock	29	57	
Options that were exercised before vesting		11	40
	7,066	5,372	4,690

Segment Information

The Company operates in a single reporting segment, the discovery, development and commercialization of RNAi therapeutics. The majority of the Company s net revenues from research collaborators was derived in the United States.

Recent Accounting Pronouncements

Effective January 1, 2008, the Company implemented SFAS 157. SFAS 157 clarifies the principle that fair value should be based on the assumptions market participants would use when pricing an asset or liability and establishes a fair value hierarchy that prioritizes the information used to develop those assumptions. Under the standard, fair value measurements would be separately disclosed by level within the fair value hierarchy. The partial adoption of SFAS 157 by the Company has had no impact on the Company s operating results or financial position. The Company is evaluating the impact, if any, full adoption of SFAS 157 will have on its nonfinancial assets and liabilities within the scope of SFAS 157.

In December 2007, the FASB reached a consensus on EITF Issue No. 07-1, *Accounting for Collaborative Arrangements* (EITF 07-1). EITF 07-1 requires collaborators to present the results of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational and consistently applied accounting policy election. Further, EITF 07-1 clarifies that the determination of whether transactions within a collaborative arrangement are part of a vendor-customer (or analogous) relationship subject to EITF 01-9. EITF 07-1 became effective on January 1, 2009. The Company is evaluating the potential impact of EITF 07-1 on its consolidated financial statements.

In December 2007, the FASB issued SFAS No. 141R, *Business Combinations* (SFAS 141R). SFAS 141R establishes principles and requirements for how an acquirer recognizes and measures in its financial statements the identifiable assets acquired, the liabilities assumed, any noncontrolling interest in the acquiree and the goodwill acquired. SFAS 141R also establishes disclosure requirements to enable the evaluation of the nature and financial effects of the business combination. SFAS 141R is effective for fiscal year 2009 and is not expected to have a material impact on the Company s consolidated financial statements.

In December 2007, the FASB issued SFAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements, an amendment of ARB No. 51* (SFAS 160). SFAS 160 changes the accounting for and reporting of noncontrolling or minority interests (now called noncontrolling interests) in consolidated financial statements. SFAS 160 became effective on January 1, 2009. When implemented, prior periods will be recast for the changes required by SFAS 160. The Company does not anticipate the adoption of SFAS 160 will have a material impact on its consolidated financial statements.

In May 2008, the FASB issued SFAS No. 162, *The Hierarchy of Generally Accepted Accounting Principles* (SFAS 162). SFAS 162 identifies the sources of accounting principles and the framework for selecting the

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

principles used (order of authority) in the preparation of financial statements that are presented in conformity with generally accepted accounting standards in the United States. The adoption of SFAS 162 did not have a material impact on the Company s consolidated financial statements.

3. SIGNIFICANT AGREEMENTS

Platform Alliances

Roche Alliance

In July 2007, the Company and, for limited purposes, Alnylam Europe, entered into a License and Collaboration Agreement (the LCA) with Roche. Under the LCA, which became effective in August 2007, the Company granted Roche a non-exclusive license to the Company s intellectual property to develop and commercialize therapeutic products that function through RNAi, subject to the Company s existing contractual obligations to third parties. The license is initially limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases, and may be expanded to include up to 18 additional therapeutic areas, comprising all other fields of human disease, as identified and agreed upon by the parties, upon payment to the Company by Roche of an additional $50.0 million for each additional therapeutic area, if any.

In consideration for the rights granted to Roche under the LCA, Roche paid the Company $273.5 million in upfront cash payments. In addition, in exchange for the Company s contributions under the LCA, for each RNAi therapeutic product successfully developed by Roche, its affiliates or sublicensees under the LCA, if any, the Company is entitled to receive milestone payments upon achievement of specified development and sales events, totaling up to an aggregate of $100.0 million per therapeutic target, together with royalty payments based on worldwide annual net sales, if any.

Under the LCA, the Company and Roche also agreed to collaborate on the discovery of RNAi therapeutic products directed to one or more disease targets (Discovery Collaboration), subject to the Company s existing contractual obligations to third parties. The collaboration between Roche and the Company will be governed by a joint steering committee for a period of five years that is comprised of an equal number of representatives from each party. In exchange for the Company s contributions to the collaboration, Roche will be required to make additional milestone and royalty payments to the Company.

The term of the LCA generally ends upon the later of ten years from the first commercial sale of a licensed product and the expiration of the last-to-expire patent covering a licensed product. After the first anniversary of the effective date, Roche may terminate the LCA, on a licensed product-by-licensed product, licensed patent-by-licensed patent, and country-by-country basis, upon 180-days prior written notice, but is required to continue to make milestone and royalty payments to the Company if any royalties were payable on net sales of a terminated licensed product during the previous 12 months. The LCA may also be terminated by either party in the event the other party fails to cure a material breach under the LCA.

In July 2007, the Company executed a Common Stock Purchase Agreement (the Common Stock Purchase Agreement) with Roche Finance Ltd, an affiliate of Roche (Roche Finance). Under the terms of the Common Stock Purchase Agreement, on August 9, 2007, Roche Finance purchased 1,975,000 shares of the Company s common stock at $21.50 per share, for an aggregate purchase price of $42.5 million. The Company recorded this issuance using the closing price of the Company s common stock on August 9, 2007, the date the shares were issued to Roche. Based on the closing price of $25.98, the fair value of the shares issued was $51.3 million, which was $8.8 million in excess of the proceeds received from Roche for the issuance of the Company s common stock. As a result, the Company allocated $8.8 million of the up-front payment from the LCA to the common stock issuance.

Under the terms of the Common Stock Purchase Agreement, in the event the Company proposes to sell or issue any of its equity securities, subject to specified exceptions, it has agreed to grant to Roche Finance the right to

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

acquire, at fair value, additional securities, such that Roche Finance would be able to maintain its ownership percentage in the Company.

In connection with the execution of the LCA and the Common Stock Purchase Agreement, the Company also executed a Share Purchase Agreement (the Alnylam Europe Purchase Agreement) with Alnylam Europe and Roche Beteiligungs GmbH, an affiliate of Roche (Roche Germany). Under the terms of the Alnylam Europe Purchase Agreement, which became effective in August 2007, the Company created a new, wholly-owned German limited liability company (Roche Kulmbach) into which substantially all of the non-intellectual property assets of Alnylam Europe were transferred, and Roche Germany purchased from the Company all of the issued and outstanding shares of Roche Kulmbach for an aggregate purchase price of $15.0 million. The Alnylam Europe Purchase Agreement also included transition services that were performed by Roche Kulmbach employees at various levels through August 2008. The Company reimbursed Roche for these services at an agreed-upon rate. The Company recorded as contra revenue (a reduction of revenues) $1.0 million and $4.2 million for these services for the years ended December 31, 2008 and 2007, respectively.

In addition, in connection with the closing of the Alnylam Europe Purchase Agreement, the Company granted restricted stock of the Company to certain employees of Roche Kulmbach. In connection with the closing, the Company also accelerated the unvested portion of the outstanding stock options of certain Alnylam Europe employees. The Company recorded $3.8 million of stock-based compensation expense during 2007 related to the restricted share grants and the stock option modifications.

In summary, the Company received upfront payments totaling $331.0 million under the Roche alliance, which include an upfront payment under the LCA of $273.5 million, $42.5 million under the Common Stock Purchase Agreement and $15.0 million for the Roche Kulmbach shares under the Alnylam Europe Purchase Agreement.

The Company recorded $278.2 million as deferred revenue in connection with the Roche alliance. This amount represents the aggregate proceeds received from Roche of $331.0 million, net of the amount allocated to the common stock issuance of $51.3 million, and the net book value of Alnylam Europe of $1.5 million.

The Company has determined that the deliverables under the Roche alliance include the license, the Alnylam Europe assets and employees, the steering committees (Joint Steering Committee and Future Technology Committee) and the services that Alnylam will be obligated to perform under the Discovery Collaboration. The Company has concluded that, pursuant to paragraph 9 of EITF 00-21, the license and assets of Alnylam Europe are not separable from the undelivered services (i.e., the steering committees and Discovery Collaboration) and, accordingly the license and the services are being treated as a single unit of accounting. When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition pattern on the final deliverable. Under the Roche alliance, the steering committee services and the Discovery Collaboration services are the final deliverables and all such services will end, contractually, five years from the effective date of the LCA. The Company is recognizing the Roche-related revenue on a straight-line basis over five years because the Company cannot reasonably estimate the total level of effort required to complete its service obligations under the LCA. The Company will continue to reassess whether it can reasonably estimate the level of effort required to fulfill its obligations under the Roche alliance. In particular, when the Discovery Collaboration commences, the Company may be able to make such an estimate. When, and if, the Company can make a reasonable estimate of its remaining efforts under the collaboration, the Company would modify its method of recognition and utilize a proportional performance method. As future substantive milestones are achieved, a portion of the milestone payment, equal to the percentage of the performance period completed when the milestone is achieved, multiplied by the amount of the milestone payment, will be recognized as revenue upon achievement of such milestone. The remaining portion of the milestone will be recognized over the remaining performance period on a straight-line basis.

In connection with the LCA and the Common Stock Purchase Agreement, the Company paid $27.5 million of license fees to the Company s licensors, primarily Isis, during 2007, in accordance with the applicable license agreements with those parties. These fees were charged to research and development expense.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Takeda Alliance

In May 2008, the Company entered into a license and collaboration agreement (the Takeda Collaboration Agreement) with Takeda to pursue the development and commercialization of RNAi therapeutics. Under the Takeda Collaboration Agreement, the Company granted Takeda a non-exclusive, worldwide, royalty-bearing license to the Company s intellectual property to develop, manufacture, use and commercialize RNAi therapeutics, subject to the Company s existing contractual obligations to third parties. The license initially is limited to the fields of oncology and metabolic disease and may be expanded at Takeda s option to include other therapeutic areas, subject to specified conditions. Under the Takeda Collaboration Agreement, Takeda will be the Company s exclusive platform partner in the Asian territory, as defined in the Takeda Collaboration Agreement, for a period of five years.

In consideration for the rights granted to Takeda under the Takeda Collaboration Agreement, Takeda agreed to pay the Company $150.0 million in upfront and near-term technology transfer payments. In addition, the Company has the option, exercisable until the start of Phase III development, to opt-in under a 50-50 profit sharing agreement to the development and commercialization in the United States of up to four Takeda licensed products, and would be entitled to opt-in rights for two additional products for each additional field expansion, if any, elected by Takeda under the Takeda Collaboration Agreement. In June 2008, Takeda paid the Company an upfront payment of $100.0 million. Takeda is also required to make the additional $50.0 million in payments to the Company upon achievement of specified technology transfer milestones, $20.0 million of which was achieved in September 2008 and paid in October 2008, $20.0 million of which is required to be paid within 12 to 24 months of execution of the Takeda Collaboration Agreement and $10.0 million of which is required to be paid within 24 to 36 months of execution of the Takeda Collaboration Agreement (collectively, the Technology Transfer Milestones). If Takeda elects to expand its license to additional therapeutic areas, Takeda will be required to pay the Company $50.0 million for each of up to approximately 20 total additional fields selected, comprising all other fields of human disease, as identified and agreed upon by the parties. In addition, for each RNAi therapeutic product developed by Takeda, its affiliates and sublicensees, if any, the Company is entitled to receive specified development and commercialization milestones, totaling up to $171.0 million per product, together with royalty payments based on worldwide annual net sales, if any.

Pursuant to the Takeda Collaboration Agreement, the Company and Takeda have also agreed to collaborate on the research of RNAi therapeutics directed to one or two disease targets agreed to by the parties (the Research Collaboration), subject to the Company s existing contractual obligations with third parties. Takeda also has the option, subject to certain conditions, to collaborate with the Company on the research and development of RNAi drug delivery technology for targets agreed to by the parties. In addition, Takeda has a right of first negotiation for the development and commercialization of the Company s RNAi therapeutic products in the Asian territory, excluding the Company s ALN-RSV01 program. In addition to the 50-50 profit sharing option, the Company has a similar right of first negotiation to participate with Takeda in the development and commercialization in the United States of licensed products. The collaboration between the Company and Takeda is governed by a joint technology transfer committee (the JTTC), a joint research collaboration committee (the JRCC) and a joint delivery collaboration committee (the JDCC), each of which is comprised of an equal number of representatives from each party.

The term of the Takeda Collaboration Agreement generally ends upon the later of (1) the expiration of the Company s last-to-expire patent covering a licensed product and (2) the last-to-expire term of a profit sharing agreement in the event the Company elects to enter into such an agreement. The Takeda Collaboration Agreement may be terminated by either party in the event the other party fails to cure a material breach under the agreement. In addition, after the first anniversary of the effective date of the Takeda Collaboration Agreement, Takeda may terminate the agreement on a licensed product-by-licensed product or country-by-country basis upon 180-days prior written notice to the Company, provided, however, that Takeda is required to continue to make royalty payments to the Company for the duration of the royalty term with respect to a licensed product.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The Company has determined that the deliverables under the Takeda agreement include the license, the joint committees (the JTTC, JRCC and JDCC), the technology transfer activities and the services that the Company will be obligated to perform under the Research Collaboration. The Company has determined that, pursuant to EITF 00-21, the license and undelivered services (i.e., the joint committees and the Research Collaboration) are not separable and, accordingly, the license and services are being treated as a single unit of accounting.

When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition pattern on the final deliverable. Under the Takeda Collaboration Agreement, the last elements to be delivered are the JDCC and JTTC services, each of which has a life of no more than seven years. The Company is recognizing the upfront payment of $100.0 million, the first Technology Transfer Milestone of $20.0 million and the $30.0 million of remaining Technology Transfer Milestones, the receipt of which the Company believes is probable, on a straight-line basis over seven years because the Company is unable to reasonably estimate the level of effort to fulfill these obligations, primarily because the effort required under the Research Collaboration is largely unknown. As future substantive milestones are achieved, a portion of the milestone payment, equal to the percentage of the performance period completed when the milestone is achieved, multiplied by the amount of the milestone payment, will be recognized as revenue upon achievement of such milestone. The remaining portion of the milestone will be recognized over the remaining performance period on a straight-line basis. The Company will continue to reassess whether it can reasonably estimate the level of effort required to fulfill its obligations under the Takeda Collaboration Agreement. When, and if, the Company can make a reasonable estimate of its remaining efforts under the collaboration, the Company would modify its method of recognition and utilize a proportional performance method.

In connection with the Takeda Collaboration Agreement, the Company paid $5.0 million of license fees to the Company s licensors, primarily Isis, during 2008, in accordance with the applicable license agreements with those parties. These fees were charged to research and development expense.

Discovery and Development Alliances

Isis Collaboration and License Agreement

In March 2004, the Company entered into a collaboration and license agreement with Isis. Isis granted the Company licenses to its current and future patents and patent applications relating to chemistry and to RNA-targeting mechanisms for the research, development and commercialization of double-stranded RNA products. The Company has the right to use Isis technologies in its development programs or in collaborations and Isis has agreed not to grant licenses under these patents to any other organization for the discovery, development and commercialization of double-stranded RNA products designed to work through an RNAi mechanism, except in the context of a collaboration in which Isis plays an active role. The Company granted Isis non-exclusive licenses to its current and future patents and patent applications relating to RNA-targeting mechanisms and to chemistry for research use. The Company also granted Isis the non-exclusive right to develop and commercialize double-stranded RNA products developed using RNAi technology against a limited number of targets. In addition, the Company granted Isis non-exclusive rights to research, develop and commercialize single-stranded RNA products.

Under the terms of the Isis agreement, the Company paid Isis an upfront license fee of $5.0 million. The Company also agreed to pay Isis milestone payments, totaling up to approximately $3.4 million, upon the occurrence of specified development and regulatory events, and royalties on sales, if any, for each product that the Company or a collaborator develops using Isis intellectual property. In addition, the Company agreed to pay to Isis a percentage of specified fees from strategic collaborations the Company may enter into that include access to the Isis intellectual property.

In conjunction with the agreement, Isis made a $10.0 million equity investment in the Company. In addition, Isis has agreed to pay the Company, per therapeutic target, a license fee of $0.5 million, and milestone payments totaling approximately $3.4 million, payable upon the occurrence of specified development and regulatory events,

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

and royalties on sales, if any, for each product developed by Isis or a collaborator that utilizes the Company s intellectual property. Isis has the right to elect up to ten non-exclusive target licenses under the agreement and has the right to purchase one additional non-exclusive target per year during the term of the collaboration.

The Isis agreement also gives the Company an option to use Isis manufacturing services for RNA-based therapeutic products. In addition, under the Isis agreement, the Company has the exclusive right to grant sub-licenses for Isis technology to third parties with whom the Company is not collaborating. The Company may include these sub-licenses in its non-exclusive platform licenses and its InterfeRx licenses. If a license includes rights to Isis intellectual property, the Company will share revenues from that license equally with Isis.

The term of the Isis agreement generally ends upon the expiration of the last-to-expire patent licensed thereunder, whether such patent is a patent licensed by the Company to Isis, or vice versa. As the license will include additional patents, if any, filed to cover future inventions, if any, the date of expiration cannot be calculated at this time.

In May 2008, as a result of certain payments received by the Company in connection with the Takeda alliance, the Company paid $4.6 million to Isis. In August 2007, as a result of certain payments received by the Company in connection with the Roche alliance, the Company paid $26.5 million to Isis. These license fees were charged to research and development expenses in the respective periods.

Novartis Broad Alliance

Beginning in September 2005, the Company entered into a series of transactions with Novartis. In September 2005, the Company and Novartis executed a stock purchase agreement (the Stock Purchase Agreement) and an investor rights agreement (the Investor Rights Agreement). In October 2005, in connection with the closing of the transactions contemplated by the Stock Purchase Agreement, the Investor Rights Agreement became effective and the Company and Novartis executed a research collaboration and license agreement (the Collaboration and License Agreement) (collectively the Novartis Agreements). The Collaboration and License Agreement had an initial term of three years, with an option for two additional one-year extensions at the election of Novartis. In July 2008, Novartis elected to extend the initial term for an additional year, through October 2009. Novartis retains the right to extend the term for a second additional year, which right must be exercised no later than July 2009. Novartis may terminate the Collaboration and License Agreement in the event that the Company materially breaches its obligations. The Company may terminate the agreement with respect to particular programs, products and or countries in the event of certain material breaches of obligations by Novartis, or in its entirety under certain circumstances for multiple such breaches.

Under the terms of the Stock Purchase Agreement, in October 2005, Novartis purchased 5,267,865 shares of the Company s common stock at a purchase price of $11.11 per share for an aggregate purchase price of $58.5 million, which, after such issuance, represented 19.9% of the Company s outstanding common stock as of the date of issuance. In addition, under the Investor Rights Agreement, the Company granted Novartis rights to acquire additional equity securities in the event that the Company proposes to sell or issue any equity securities, subject to specified exceptions, as described in the Investor Rights Agreement, such that Novartis would be able to maintain its then-current ownership percentage in the Company s outstanding common stock. Pursuant to terms of the Investor Rights Agreement, in May 2008, Novartis purchased 213,888 shares of the Company s common stock at a purchase price of $25.29 per share resulting in a payment to the Company of $5.4 million. At December 31, 2008, Novartis owned

13.2% of the Company s outstanding common stock.

Under the terms of the Collaboration and License Agreement, the parties will work together on a defined number of selected targets, as defined in the Collaboration and License Agreement, to discover and develop therapeutics based on RNAi. In consideration for the rights granted to Novartis under the Collaboration and License Agreement, Novartis made upfront payments totaling $10.0 million to the Company in October 2005, partly to reimburse prior costs incurred by the Company to develop *in vivo* RNAi technology. The Collaboration and License Agreement also includes terms under which Novartis will provide the Company with research funding and

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

milestone payments as well as royalties on annual net sales of products resulting from the Collaboration and License Agreement, if any. The amount of research funding provided by Novartis under the Collaboration and License Agreement during the research term is dependent upon the number of active programs on which the Company is collaborating with Novartis at any given time and the number of Company employees that are working on those programs, in respect of which Novartis reimburses the Company at an agreed upon rate. Under the terms of the Collaboration and License Agreement, Novartis has the right to select up to 30 exclusive targets to include in the collaboration, which number may be increased to 40 under certain circumstances and upon additional payments. For RNAi therapeutic products successfully developed under the Collaboration and License Agreement, if any, the Company would be entitled to receive milestone payments upon achievement of certain specified development and annual net sales events, up to an aggregate of $75.0 million per therapeutic product.

Under the terms of the Collaboration and License Agreement, the Company retains the right to discover, develop, commercialize and manufacture compounds that function through the mechanism of RNAi, or products that contain such compounds as an active ingredient, with respect to targets not selected by Novartis for inclusion in the collaboration, provided that Novartis has a right of first offer with respect to an exclusive license for additional targets before the Company partners any of those additional targets with third parties.

Novartis may exercise this Integration Option at any point during the research term, as defined in the Collaboration and License Agreement. The research term expires in October 2009 and may be extended until October 2010 at Novartis election. In connection with the exercise of the Integration Option, Novartis would be required to make additional payments to the Company totaling $100.0 million, payable in full at the time of exercise, which payments would include an option exercise fee, a milestone based on the overall success of the collaboration and pre-paid milestones and royalties that could become due as a result of future development of products using the Company s technology. In addition, under this license grant, Novartis may be required to make milestone and royalty payments to the Company in connection with the successful development and commercialization of RNAi therapeutic products, if any. The license grant under the integration option, if exercised by Novartis, would be structured similarly to the Company s non-exclusive platform licenses with Roche and Takeda.

The Company initially deferred the non-refundable $10.0 million upfront payment and the $6.4 million premium received that represents the difference between the purchase price and the closing price of the common stock of the Company on the date of the stock purchase from Novartis. These payments, in addition to research funding and certain milestone payments, the receipt of which is considered probable, are being amortized into revenue using the proportional performance method over the estimated duration of the Novartis agreement or ten years. Under this model, the Company estimates the level of effort to be expended over the term of the agreement and recognizes revenue based on the lesser of the amount calculated based on proportional performance of total expected revenue or the amount of non-refundable payments earned.

As future substantive milestones are achieved, and to the extent they are within the period of performance, milestone payments will be recognized as revenue on a proportional performance basis over the contract s entire performance period, starting with the contract s commencement. A portion of the milestone payment, equal to the percentage of total performance completed when the milestone is achieved, multiplied by the milestone payment, will be recognized as revenue upon achievement of the milestone. The remaining portion of the milestone will be recognized over the remaining performance period under the proportional performance method.

The Company believes the estimated period of performance under the Novartis agreement includes the three-year term of the agreement, two one-year extensions at the election of Novartis and limited support as part of a technology transfer until the fifth anniversary of the termination of the agreement. In July 2008, Novartis elected to extend the initial term for an additional year, through October 2009. The Company continues to use an expected term of ten years in its proportional performance model. The Company reevaluates the expected term when new information is known that could affect the Company s estimate. In the event the Company s period of performance is different than estimated, revenue recognition will be adjusted on a prospective basis.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Novartis Pandemic Flu Alliance

In February 2006, the Company entered into an alliance with Novartis for the development of RNAi therapeutics for pandemic flu (Novartis Flu Agreement). Under the terms of the Novartis Flu Agreement, the Company and Novartis have joint responsibility for development of RNAi therapeutics for pandemic flu. This program was stopped and currently there are no specific resource commitments for this program.

Biogen Idec Collaboration Agreement

In September 2006, the Company entered into a Collaboration and License Agreement (the Biogen Idec Collaboration Agreement) with Biogen Idec focused on the discovery and development of therapeutics based on RNAi for the potential treatment of progressive multifocal leukoencephalopathy (PML). Under the terms of the Biogen Idec Collaboration Agreement, the Company granted Biogen Idec an exclusive license to distribute, market and sell certain RNAi therapeutics to treat PML and Biogen Idec has agreed to fund all related research and development activities. The Company received an upfront $5.0 million payment from Biogen Idec. In addition, upon the successful development and utilization of a product resulting from the collaboration, if any, Biogen Idec would be required to pay the Company milestone payments, totaling $51.0 million, and royalty payments on sales, if any. The Company is recognizing revenue under the Biogen Idec collaboration on a straight-line basis over five years because the Company cannot reasonably estimate the total level of effort required to fulfill its obligations under this collaboration. The pace and scope of future development of this program is the responsibility of Biogen Idec.

Unless earlier terminated, the Biogen Idec agreement will remain in effect until the expiration of all payment obligations under the agreement. Either the Company or Biogen Idec may terminate the agreement in the event that the other party breaches its obligations thereunder. Biogen Idec may also terminate the agreement, on a country-by-country basis, without cause upon 90 days prior written notice.

Merck Agreement

In July 2006, the Company executed an Amended and Restated Research Collaboration and License Agreement (the Amended License Agreement) with Merck. In September 2007, the Company and Merck terminated the Amended License Agreement (the Termination Agreement). Pursuant to the Termination Agreement, all license grants of intellectual property to develop, manufacture and/or commercialize RNAi therapeutic products under the Amended License Agreement ceased as of the date of the Termination Agreement, subject to certain specified exceptions. The Termination Agreement further provides that, subject to certain conditions, the Company and Merck will each retain sole ownership and rights in their own intellectual property. The Company has no remaining deliverables under the Amended License Agreement. The Company was recognizing the remaining deferred revenue of $3.5 million under the Amended License Agreement, related to upfront cash payments and additional license fee payments received from Merck, on a straight-line basis over the remaining period of expected performance of four years. As a result of the Termination Agreement, the Company recognized this remaining deferred revenue of $3.5 million during 2007.

Product Alliances

Kyowa Hakko Alliance

In June 2008, the Company entered into a License and Collaboration Agreement (the Kyowa Hakko Agreement) with Kyowa Hakko. Under the Kyowa Hakko Agreement, the Company granted Kyowa Hakko an exclusive license to its intellectual property in Japan and other markets in Asia (the Licensed Territory) for the development and commercialization of ALN-RSV01, an RNAi therapeutic for the treatment of respiratory syncytial virus (RSV) infection, for which the Company is currently conducting Phase II clinical trials. The Kyowa Hakko Agreement also covers additional RSV-specific RNAi therapeutic compounds that comprise the

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

ALN-RSV program (Additional Compounds). The Company retains all development and commercialization rights worldwide excluding the Licensed Territory.

Under the terms of the Kyowa Hakko Agreement, in June 2008, Kyowa Hakko paid the Company an upfront cash payment of $15.0 million. In addition, Kyowa Hakko is required to make payments to the Company upon achievement of specified development and sales milestones totaling up to $78.0 million, and royalty payments based on annual net sales, if any, of ALN-RSV01 by Kyowa Hakko, its affiliates and sublicensees in the licensed territory.

The collaboration between Kyowa Hakko and the Company is governed by a joint steering committee that is comprised of an equal number of representatives from each party. Under the agreement, Kyowa Hakko is establishing a development plan for ALN-RSV01 relating to the development activities to be undertaken in the Licensed Territory, with the initial focus on Japan. Kyowa Hakko is responsible, at its expense, for all development activities under the development plan that are reasonably necessary for the regulatory approval and commercialization of ALN-RSV01 in Japan and the rest of the Licensed Territory. The Company will be responsible for supply of the product to Kyowa Hakko under a supply agreement unless Kyowa Hakko elects, prior to the first commercial sale of the product in the Licensed Territory, to manufacture the product itself or arrange for a third party to manufacture the product.

The term of the Kyowa Hakko agreement generally ends on a country-by-country basis upon the later of (1) the expiration of the Company s last-to-expire patent covering a licensed product and (2) the tenth anniversary of the first commercial sale in the country of sale. Additional patent filings relating to the collaboration may be made in the future. The Kyowa Hakko agreement may be terminated by either party in the event the other party fails to cure a material breach under the agreement. In addition, Kyowa Hakko may terminate the agreement without cause upon 180-days prior written notice to the Company, subject to certain conditions.

The Company has determined that the deliverables under the Kyowa Hakko Agreement include the license, the joint steering committee, the manufacturing services and any Additional Compounds. The Company has determined that, pursuant to EITF 00-21, the individual deliverables are not separable and, accordingly, must be accounted for as a single unit of accounting.

When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition pattern on the final deliverable. The Company is currently unable to reasonably estimate its period of performance under the Kyowa Hakko Agreement, as it is unable to estimate the timeline of its deliverables related to the fixed-price option granted to Kyowa Hakko for any Additional Compounds. The Company is deferring all revenue under the Kyowa Hakko Agreement until it is able to reasonably estimate its period of performance. The Company will continue to reassess whether it can reasonably estimate the period of performance to fulfill its obligations under the Kyowa Hakko Agreement.

Government Funding

NIH Contract

In September 2006, NIAID awarded the Company a contract for up to $23.0 million over four years to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus, including the Ebola virus. Of the $23.0 million in funding, the government initially committed to pay the Company up to $14.2 million over the first two years of the contract. In June 2008, as a result of the progress of the program, the government awarded the Company an additional $7.5 million, to be paid through September 2009 for the third year of the contract, together with any remaining funds carried over from the funding allocated for the first two years of the contract. The Company recognizes revenue under government cost reimbursement contracts as it performs the underlying research and development activities.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Department of Defense Contract

In August 2007, DTRA awarded the Company a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus. The government initially committed to pay the Company up to $10.9 million through February 2009, which included a six-month extension granted by DTRA in July 2008. Following a program review in early 2009, the Company and DTRA have determined to end this program and accordingly, the remaining funds of up to $27.7 million will not be accessed. The Company recognizes revenue under government cost reimbursement contracts as it performs the underlying research and development activities.

Delivery Technology

The Company is working to extend its capabilities in developing technology to achieve efficacious and safe delivery of RNAi therapeutics to a broad spectrum of organ and tissue types. In connection with these efforts, the Company has entered into a number of agreements to evaluate and gain access to certain delivery technologies. In some instances, the Company is also providing funding to support the advancement of these delivery technologies.

In January 2007, the Company obtained an exclusive worldwide license to the liposomal delivery formulation technology of Tekmira for the discovery, development and commercialization of lipid-based nanoparticle formulations for the delivery of RNAi therapeutics. In connection with its original agreement with Tekmira, the Company issued to Tekmira 361,990 shares of common stock. These shares had a value of $7.9 million at the time of issuance, which amount was expensed during the first quarter of 2007. In May 2008, Tekmira acquired Protiva Biotherapeutics Inc. (Protiva). In connection with this acquisition, the Company entered into new agreements with Tekmira and Protiva which provide the Company with access to key existing and future technology and intellectual property for the systemic delivery of RNAi therapeutics with liposomal delivery technologies. In addition, the Company made an equity investment of $5.0 million in Tekmira, purchasing 2,083,333 shares of Tekmira common stock at a price of $2.40 per share, which represented a premium of $1.00 per share, or an aggregate of $2.1 million. This premium was calculated as the difference between the purchase price and the closing price of Tekmira s common stock on the effective date of the acquisition. The Company allocated this $2.1 million premium to the expansion of the Company s access to key technology and intellectual property rights and, accordingly, recorded a charge to research and development expense during the second quarter of 2008. The Company recorded this investment as an available-for-sale security in marketable securities on its consolidated balance sheets. During the year ended December 31, 2008, the Company recorded an impairment charge of $1.6 million related to its investment in Tekmira, as the decrease in the fair value of this investment was deemed to be other than temporary. In connection with these transactions, the Company and Tekmira cancelled the Company s $5.0 million capital equipment loan to Tekmira, which was never drawn down by Tekmira.

4. INTANGIBLE ASSETS

Intangible assets at December 31, 2008 and 2007 are as follows, in thousands:

	December 31,	
	2008	2007

Core Technology	$ 2,410	$ 2,410
Less accumulated amortization:	(1,615)	(1,442)
	$ 795	$ 968

During the years ended December 31, 2008, 2007 and 2006, the Company recorded $0.2 million, $0.3 million and $0.4 million, respectively, of amortization expense related to its core technology and workforce intangibles, of which the entire amount is included in research and development expenses. Workforce intangibles were fully amortized during 2007. Core technology is being amortized over its estimated useful life of ten years through 2013.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

During 2007, the Company reduced its intangible assets by $0.6 million as a result of the realization of pre-acquisition deferred tax assets associated with net operating loss carryforwards.

5. PROPERTY AND EQUIPMENT

Property and equipment consist of the following at December 31, 2008 and 2007, in thousands:

		December 31,	
	Useful Life	**2008**	**2007**
Laboratory equipment	5 years	$ 12,617	$ 7,963
Computer equipment and software	3 years	2,653	2,080
Furniture and fixtures	5 years	1,532	1,271
Leasehold improvements	*	18,126	9,172
Construction in progress		23	3,702
		34,951	24,188
Less: accumulated depreciation		(15,757)	(10,378)
		$ 19,194	$ 13,810

* shorter of asset life or lease term

Depreciation expense was $5.4 million, $3.8 million and $3.4 million for the years ended December 31, 2008, 2007 and 2006, respectively.

6. NOTES PAYABLE

Equipment Lines of Credit

In March 2006, the Company entered into an agreement with Oxford Finance Corporation (Oxford) to establish an equipment line of credit for up to $7.0 million to help support capital expansion of the Company s facility in Cambridge, Massachusetts and capital equipment purchases. The agreement allowed the Company to draw down amounts under the line of credit through December 31, 2007 upon adherence to certain conditions. During 2006 and 2007, the Company borrowed an aggregate of $5.2 million from Oxford pursuant to the agreement at fixed rates ranging from 10.0% to 10.4%. In December 2008, the Company defeased the outstanding balance of $1.7 million under the Oxford line of credit.

In March 2004, the Company entered into an agreement with Lighthouse Capital Partners V, L.P. (Lighthouse) to establish an equipment line of credit for $10.0 million. In June 2005, the parties amended the agreement to allow the Company the ability to draw down amounts under the line of credit through December 31, 2005 upon adherence to certain conditions. Interest on the outstanding principal balance accrued at fixed rates of 9.25% to 10.25%. On the maturity of each equipment advance under the line of credit, the Company was required to pay, in addition to the principal and interest due, an additional amount of 11.5% of the original principal. This amount was accrued over the applicable borrowing period as additional interest expense. In December 2008, the Company defeased the outstanding balance of $2.2 million under the Lighthouse line of credit.

At December 31, 2008, the Company had no outstanding debt.

7. COMMITMENTS AND CONTINGENCIES

Indemnifications

Licensor indemnification In connection with a certain license agreement, the Company is required to indemnify the licensor for certain damages arising in connection with the intellectual property rights licensed under

ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

the agreement. The Company believes that the probability of receiving a claim is remote and, as such, no amounts have been accrued related to this indemnification at December 31, 2008 and 2007.

The Company is also a party to a number of agreements entered into in the ordinary course of business, which contain typical provisions, which obligate the Company to indemnify the other parties to such agreements upon the occurrence of certain events. Such indemnification obligations are usually in effect from the date of execution of the applicable agreement for a period equal to the applicable statute of limitations. The aggregate maximum potential future liability of the Company under such indemnification provisions is uncertain. Since its inception, the Company has not incurred any expenses as a result of such indemnification provisions. Accordingly, the Company has determined that the estimated aggregate fair value of its potential liabilities under such indemnification provisions is minimal and has not recorded any liability related to such indemnification provisions at December 31, 2008 and 2007.

Technology License Commitments

The Company has licensed from third parties the rights to use certain technologies in its research process as well as in any products the Company may develop including these licensed technologies. In accordance with the related license agreements, the Company is required to make certain fixed payments to the licensor or a designee of the licensor over various agreement terms. Many of these agreement terms are consistent with the remaining lives of the underlying intellectual property that the Company has licensed. At December 31, 2008, the Company was committed to make the following fixed license payments under existing license agreements, in thousands:

Year Ending December 31,	
2009	$ 3,612
2010	2,552
2011	2,539
2012	1,507
2013	415
Thereafter	5,700
Total	$ 16,325

Operating Leases

The Company leases office and laboratory space in Cambridge, Massachusetts for its corporate headquarters under non-cancelable operating lease agreements. The Company also had a lease in Kulmbach, Germany through August 2007. Total rent expense, including operating expenses, under these operating leases was $4.6 million, $4.7 million and $2.6 million, for the years ended December 31, 2008, 2007 and 2006, respectively.

In 2003, the Company entered into an operating lease to rent laboratory and office space in Cambridge, Massachusetts through September 2011. In March 2006, the Company amended its lease agreement to rent additional space in this same facility. The Company has the option to extend the lease for two successive five-year extensions.

Pursuant to the terms of the lease agreement, the Company secured a $2.3 million letter of credit as security for its leased facility. The underlying cash securing this letter of credit has been classified as long-term restricted cash in the accompanying consolidated balance sheets.

In October 2007, the Company subleased from Archemix Corp. (Archemix) 22,456 rentable square feet of office and laboratory space in the same location as the Company s corporate headquarters (the Sublease). The initial term of the Sublease will expire in September 2011, and the Company holds an option to extend the lease for an additional 48-month period, subject to certain termination rights granted to each of the Company and Archemix.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

In addition and in connection with the execution of the Sublease, the Company issued a letter of credit in favor of Archemix in the amount of $0.8 million. The underlying cash securing this letter of credit has been classified as long-term restricted cash in the accompanying consolidated balance sheets.

The Company received $7.3 million in leasehold improvement incentives from its landlords in connection with its leases. These leasehold improvement incentives are being accounted for as a reduction in rent expense ratably over the lease term. The balance from these leasehold improvement incentives is included in current portion of deferred rent and deferred rent, net of current portion in the balance sheets at December 31, 2008 and 2007.

In connection with the Roche alliance in August 2007, Roche purchased the assets of Alnylam Europe, which included the lease for the facility in Kulmbach, Germany.

Future minimum lease payments under these non-cancelable leases are approximately as follows, in thousands:

Year Ending December 31,	
2009	$ 3,296
2010	3,296
2011	2,472
Total	$ 9,064

Legal Proceedings

The Company may periodically become subject to legal proceedings and claims arising in connection with on-going business activities, including being subject to claims or disputes related to patents that have been issued or are pending in the field of research the Company is focused on. The Company does not believe that there were any material claims against the Company at December 31, 2008.

8. STOCKHOLDERS EQUITY

Preferred Stock

The Company has authorized up to 5,000,000 shares of preferred stock, $0.01 par value per share, for issuance. The preferred stock will have such rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, as shall be determined by the Company s Board of Directors upon its issuance. At December 31, 2008 and 2007, there were no shares of preferred stock outstanding.

Stockholder Rights Agreement

On July 13, 2005, the Board of Directors of the Company declared a dividend of one right (collectively, the Rights) to buy one one-thousandth of a share of newly designated Series A Junior Participating Preferred Stock (Series A Junior

Preferred Stock) for each outstanding share of the Company s common stock to stockholders of record at the close of business on July 26, 2005. Initially, the Rights are not exercisable and will be attached to all certificates representing outstanding shares of common stock, and no separate Rights Certificates will be distributed. The Rights will expire at the close of business on July 13, 2015 unless earlier redeemed or exchanged. Until a right is exercised, the holder thereof, as such, will have no rights as a stockholder of the Company, including the right to vote or to receive dividends. The rights are not immediately exercisable. Subject to the terms and conditions of the Rights Agreement entered into by the Company with Computershare (formerly EquiServe Trust Company, N.A.), as Rights Agent (the Rights Agreement), the Rights will become exercisable upon the earlier of (1) 10 business days following the later of (a) the first date of a public announcement that a person or group (an Acquiring Person) acquires, or obtained the right to acquire, beneficial ownership of 20 percent or

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

more of the outstanding shares of common stock of the Company or (b) the first date on which an executive officer of the Company has actual knowledge that an Acquiring Person has become such or (2) 10 business days following the commencement of a tender offer or exchange offer that would result in a person or group beneficially owning more than 20 percent of the outstanding shares of common stock of the Company. Each right entitles the holder to purchase one one-thousandth of a share of Series A Junior Preferred Stock at an initial purchase price of $80.00 in cash, subject to adjustment. In the event that any person or group becomes an Acquiring Person, unless the event causing the 20% threshold to be crossed is a Permitted Offer (as defined in the Rights Agreement), each Right not owned by the Acquiring Person will entitle its holder to receive, upon exercise, that number of shares of common stock of the Company (or in certain circumstances, cash, property or other securities of the Company) which equals the exercise price of the Right divided by 50% of the current market price (as defined in the Rights Agreement) per share of such common stock at the date of the occurrence of the event. In the event that, at any time after any person or group becomes an Acquiring Person, (i) the Company is consolidated with, or merged with and into, another entity and the Company is not the surviving entity of such consolidation or merger (other than a consolidation or merger which follows a Permitted Offer) or if the Company is the surviving entity, but shares of its outstanding common stock are changed or exchanged for stock or securities (of any other person) or cash or any other property, or (ii) more than 50% of the Company s assets or earning power is sold or transferred, each holder of a Right (except Rights which previously have been voided as set forth in the Rights Agreement) shall thereafter have the right to receive, upon exercise, that number of shares of common stock of the acquiring company which equals the exercise price of the Right divided by 50% of the current market price of such common stock at the date of the occurrence of the event.

Public Offerings of Common Stock

In January 2006, the Company completed a public offering of its common stock. The public offering consisted of the sale and issuance of 5,115,961 shares of the Company s common stock. The price to the public was $13.00 per share, and proceeds to the Company from the offering, net of expenses, were approximately $62.2 million. The shares of common stock were registered pursuant to registration statements filed with the SEC in 2006 and 2005.

In December 2006, the Company completed a public offering of its common stock. The public offering consisted of the sale and issuance of 4,700,000 shares of the Company s common stock. The price to the public was $22.00 per share, and proceeds to the Company from the offering, net of expenses, were approximately $101.1 million. The shares of common stock were registered pursuant to a registration statement filed with the SEC in November 2006.

9. STOCK INCENTIVE PLANS

Stock Plans

As of December 31, 2008, the Company s 2004 Stock Incentive Plan, as amended (the 2004 Plan), provides for the granting of restricted stock awards and stock options to purchase up to 10,295,794 shares of common stock. The 2004 Plan provides for an annual increase in the number of shares available for issuance under the plan equal to the lesser of 2,631,578 shares of common stock, 5% of the Company s outstanding shares or an amount determined by the Board of Directors. In addition, the 2004 Plan includes a non-employee director stock option program under which each eligible non-employee director is entitled to (1) a grant of an option to purchase 30,000 shares of common stock upon his or her initial appointment to the Board of Directors, or such other amount as the Board of Directors deems appropriate, and (2) a subsequent annual grant of an option to purchase 15,000 shares of common stock based on continued service, made on the date of each annual meeting of stockholders, provided the non-employee director has served as a director for at least six months and is serving as a director immediately prior to and following such annual meeting. The chairman of the audit committee will receive an additional annual grant of an option to purchase 10,000 shares of common stock based on continued service. Stock options granted by the Company to non-employee directors (i) upon their appointment to the Board of Directors vest as to one-third of such

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

shares on each of the first, second and third anniversaries of the date of grant and (ii) at each year s annual meeting at which they serve as a director vest in full on the first anniversary of the date of grant.

At December 31, 2008, an aggregate of 7,560,298 shares of common stock were reserved for issuance under the Company s stock plans, including outstanding options to purchase 7,037,214 shares of common stock and 523,084 shares were available for future grant under the 2004 Plan. Each option shall expire within 10 years of issuance. Stock options granted by the Company generally vest as to 25% of the shares on the first anniversary of the grant date and 6.25% of the shares at the end of each successive three-month period until fully vested.

Stock-Based Compensation

Effective January 1, 2006, the Company adopted the fair value recognition provisions of SFAS 123R using the modified-prospective-transition method. Under the provisions of SFAS 123R, the Company recorded $14.3 million, $11.9 million and $6.1 million of stock-based compensation for the years ended December 31, 2008, 2007 and 2006, respectively, related to employee stock options and the employee stock purchase plan.

The Company accounts for non-employee grants as an expense over the vesting period of the underlying stock options using the method prescribed by FIN 28. At the end of each financial reporting period prior to vesting, the value of these options (as calculated using the Black-Scholes option-pricing model) is re-measured using the then-current fair value of the Company s common stock. The Company recognized $2.1 million, $2.6 million and $2.2 million of non-employee stock-based compensation expense for the years ended December 31, 2008, 2007 and 2006, respectively.

The Company granted the members of the Regulus Therapeutics scientific advisory board and board of directors options to purchase 30,000 and 68,500 shares of common stock during 2008 and 2007, respectively. In addition, the Company granted options to purchase 60,000 shares of common stock to two officers of Regulus Therapeutics during 2008 and 60,000 shares of common stock to the chief executive officer of Regulus Therapeutics in 2007. In addition to the total stock-based compensation expense stated above, the Company recorded $1.6 million and $0.2 million of stock-based compensation expense related to these option grants in equity in loss of joint venture in its consolidated statements of operations for the years ended December 31, 2008 and 2007, respectively, using the method prescribed by FIN 28.

In connection with the closing of the sale of Alnylam Europe to Roche, the Company granted 95,109 shares of restricted stock of the Company to certain employees of Roche Kulmbach. In connection with the closing, the Company also accelerated 177,233 of unvested outstanding stock options of certain Alnylam Europe employees. The Company recorded $3.8 million of stock-based compensation expense during 2007 related to the restricted stock grants and the stock option modifications.

Total compensation cost for all stock-based payment arrangements for the years ended December 31, 2008, 2007 and 2006 was $18.0 million, $14.7 million and $8.3 million, respectively. No amounts relating to the stock-based compensation have been capitalized.

Valuation Assumptions for Stock Plans and Employee Stock Purchase Plan

The fair value of stock options at date of grant, based on the following assumptions, was estimated using the Black-Scholes option-pricing model. The Company s expected stock-price volatility assumption for 2008 and the three months ended December 31, 2007 is based on a combination of implied volatilities of its publicly traded stock option prices as well as the historical volatility of the Company s publicly traded stock. During the nine months ended September 30, 2007 and during 2006, the Company s expected stock-price volatility assumption was based on a combination of implied volatilities of similar entities whose share or option prices are publicly available as well as the historical volatility of the Company s publicly traded stock. The expected life assumption for 2008 and for the three months ended December 31, 2007 is based on the equal weighting of the Company s historical data and the historical data of the Company s pharmaceutical and biotechnology peers. During the nine months ended

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

September 30, 2007 and during 2006, the expected life assumption is based on the simplified method provided for under SAB No. 107 (SAB 107), which averages the contractual term of the Company s options (ten years) with the ordinary vesting term (2.2 years). The dividend yield assumption is based on the fact that the Company has never paid cash dividends and has no present intention to pay cash dividends. The risk-free interest rate used for each grant is equal to the zero coupon rate in effect at the time of grant for instruments with a similar expected life. The Company currently expects, based on an analysis of its historical forfeitures, that approximately 86% of its options will actually vest, and therefore have applied an annual forfeiture rate of 3.7% to all unvested options as of December 31, 2008. The Company will record additional expense if the actual forfeitures are lower than estimated and will record a recovery of prior expense if the actual forfeitures are higher than estimated.

	2008	2007	2006
Risk-free interest rate	1.5-3.5%	4.4-4.7%	4.70%
Expected dividend yield			
Expected option life	5.7-6.3 years	6.0-6.1 years	6.1 years
Expected volatility	66-67%	64-67%	67%

At December 31, 2008, there remained $50.0 million of unearned compensation expense related to unvested employee stock options to be recognized as expense over a weighted-average period of approximately 1.6 years.

Stock Option Activity

The following table summarizes the activity of the Company s stock option plans:

	Number of Options	Weighted Average Exercise Price
Outstanding, December 31, 2007	5,304,021	$ 17.18
Granted	2,155,056	$ 24.87
Exercised	(377,228)	$ 10.04
Cancelled	(44,635)	$ 25.19
Outstanding, December 31, 2008	7,037,214	$ 19.87
Exercisable at December 31, 2006	1,953,502	$ 4.44
Exercisable at December 31, 2007	1,913,468	$ 7.49
Exercisable at December 31, 2008	2,903,479	$ 12.87

The weighted average remaining contractual life for options outstanding and exercisable at December 31, 2008 was 8.1 years and 6.8 years, respectively.

The aggregate intrinsic value of outstanding options at December 31, 2008 was $48.3 million, of which $37.2 million related to exercisable options. The intrinsic value of options exercised was $8.2 million, $24.6 million and $7.6 million for the years ended December 31, 2008, 2007 and 2006, respectively. The weighted average fair value of stock options granted as part of the 2004 Plan was $15.02, $16.58 and $12.95 per share for the years ended December 31, 2008, 2007 and 2006, respectively.

The aggregate intrinsic value of options expected to vest at December 31, 2008 was $10.6 million. The weighted average fair value of stock options expected to vest as part of the 2004 Plan was $12.10 per share as of December 31, 2008. The weighted average remaining contractual life for options expected to vest at December 31, 2008 was 9.0 years and the weighted average exercise price for these options was $24.76 per share.

ALNYLAM PHARMACEUTICALS, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Restricted Stock Awards

The following table summarizes the activity of the Company s restricted stock awards:

	Number of Awards	Weighted Average Grant Date Fair Value
Unvested at December 31, 2007	57,049	$ 25.98
Granted		$
Vested	(28,531)	$ 25.98
Forfeited		$
Unvested at December 31, 2008	28,518	$ 25.98

The total fair value of restricted stock awards that vested during the year ended December 31, 2008 and 2007 was $0.7 million and $1.0 million, respectively. The weighted average remaining contractual life for restricted stock awards at December 31, 2008 was 1.0 years.

Employee Stock Purchase Plan

In 2004, the Company adopted the 2004 Employee Stock Purchase Plan (the 2004 Purchase Plan) with 315,789 shares authorized for issuance. Under the 2004 Purchase Plan as adopted, the Company made one offering each year, at the end of which employees could purchase shares of common stock through payroll deductions made over the term of the offering. Initially, the annual offering period began on the 1st day of November each year and ended on the 31st day of October the following year. In June 2007, the Compensation Committee of the Board of Directors amended the offering period of the 2004 Purchase Plan to provide that each offering period will be for a period of six months, beginning with the offering period commencing on November 1, 2007. The per-share purchase price at the end of the offering is equal to the lesser of 85% of the closing price of the common stock at the beginning or end of the offering period. The Company issued 35,065, 29,723 and 40,530 shares during 2008, 2007 and 2006, respectively, and as of December 31, 2008, 158,679 shares were available for issuance under the 2004 Purchase Plan.

The weighted average fair value of stock purchase rights granted as part of the 2004 Purchase Plan was $9.51, $10.61 and $8.16 for the years ended December 31, 2008, 2007 and 2006, respectively. The fair value was estimated using the Black-Scholes option-pricing model. The Company used a weighted-average stock-price volatility of 66%, expected option life assumption of one year and risk-free interest rate of 2.9%. The Company recorded $0.3 million, $0.2 million and $0.2 million of stock-based compensation for the years ended December 31, 2008, 2007 and 2006, respectively, related to the 2004 Purchase Plan.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

10. INCOME TAXES

Deferred income taxes reflect the tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting and income tax purposes. A valuation allowance is established when uncertainty exists as to whether all or a portion of the net deferred tax assets will be realized. Components of the net deferred tax asset (liability) as of December 31, 2008, 2007 and 2006 are as follows, in thousands:

	2008	2007	2006
Deferred tax assets:			
Net operating loss carryforwards	$ 298	$ 49,910	$ 21,656
Research and development credits	496	3,582	3,456
Foreign tax credits		3,072	
Capitalized research and development and start-up costs	9,558	12,750	13,674
Deferred revenue	74,423	2,745	7,211
Deferred compensation	7,532	3,237	1,731
Intangible assets	5,422	1,540	3,100
Other	2,686	3,674	1,706
Total deferred tax assets	100,415	80,510	52,534
Deferred tax liabilities:			
Intangible assets	(246)	(365)	(1,004)
Deferred tax asset valuation allowance	(95,033)	(80,510)	(50,863)
Net deferred tax asset (liability)	$ 5,136	$ (365)	$ 667

The provision for income taxes for the years ended December 31, 2008 and 2007 was as follows, in thousands:

	2008	2007
U.S.:		
Current	$ 5,978	$
Deferred	(5,382)	
Total U.S.	596	
Foreign:		
Current	242	3,356
Deferred	(119)	1,889
Total Foreign	123	5,245

Provision for income taxes	$ 719	$ 5,245

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The Company s effective income tax rate differs from the statutory federal income tax rate as follows for the years ended December 31, 2008, 2007 and 2006:

	2008	**2007**	**2006**
At U.S. federal statutory rate	35.0%	34.0%	34.0%
State taxes, net of federal effect	(0.5)	5.8	5.3
Foreign tax credit		3.8	
Foreign dividends		(6.6)	
Stock compensation	(6.0)	(2.4)	
Other	(0.3)		
Other permanent items	(0.3)	1.6	(5.4)
Deemed gain on Roche Germany transaction		(6.3)	
Research credits		0.4	4.2
Valuation allowance	(30.7)	(36.7)	(38.0)
Effective income tax rate	(2.8)%	(6.4)%	0.1%

As required by SFAS No. 109, *Accounting for Income Taxes,* management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Management has concluded, in accordance with the applicable accounting standards, that it is more likely than not that the Company may not realize the benefit of all its deferred tax assets. Accordingly, a valuation allowance has been recorded against the deferred tax assets that management believes will not be realized. Management reevaluates the positive and negative evidence on a quarterly basis. The valuation allowance increased by $14.5 million, $29.6 million and $13.2 million for the years ended December 31, 2008, 2007 and 2006, respectively, due primarily to net operating loss carryforwards and deferred revenue.

During 2008, the Company utilized certain tax attributes, including net operating loss and tax credit carryforwards as a result of the recognition of revenue for certain proceeds received from the Roche alliance. However, the Company also generated a deferred tax asset related to the recognition of this revenue for tax purposes. As a result, the Company has recorded a net deferred tax asset to the extent it is more likely than not that the asset will be realized. The remaining deferred tax assets are subject to a valuation allowance as it is more likely than not that those assets will not be realized.

The deferred tax assets above exclude $9.4 million of deductions related to the exercise of stock options subsequent to the adoption of SFAS 123R. This amount represents an excess tax benefit as defined under SFAS 123R and has not been included in the gross deferred tax assets.

At December 31, 2008, the state net operating loss carryforward was $8.6 million and the state research and development tax credit carryforward was $0.5 million. These attributes are available to reduce future tax liabilities and expire at various dates through 2023. Ownership changes, as defined in the Internal Revenue Code, including those resulting from the issuance of common stock in connection with the Company s public offerings, may limit the amount of net operating loss and tax credit carryforwards that can be utilized to offset future taxable income or tax liability. The Company has determined that there is no limitation on the utilization of net operating loss and tax credit carryforwards in accordance with Section 382 of the Internal Revenue Code in 2008.

On January 1, 2007, the Company adopted the provisions of FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes an interpretation of FASB Statement 109* (FIN 48), which was issued in July 2006. The implementation of FIN 48 did not result in any adjustment to the Company s beginning tax positions. The Company continues to recognize fully its tax benefits which are offset by a valuation allowance to the extent that it is more likely than not that the deferred tax assets will not be realized. At December 31, 2008, the Company had an unrecognized tax benefit of $0.2 million.

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The tax years 2002 through 2006 remain open to examination by major taxing jurisdictions to which the Company is subject, which are primarily in the United States, as carryforward attributes generated in years past may still be adjusted upon examination by the Internal Revenue Service or state tax authorities if they have or will be used in a future period. The Company is currently not under examination by the Internal Revenue Service or any other jurisdictions for any tax years. The Company recognizes both accrued interest and penalties related to unrecognized benefits in income tax expense. The Company has not recorded any interest and penalties on any unrecognized tax benefits since its inception.

11. 401(K) SAVINGS PLAN

The Company sponsors a savings plan for its employees in the United States, who meet certain eligibility requirements, which is designed to be a qualified plan under section 401(k) of the Internal Revenue Code (the 401(k) Plan). Participants may contribute up to 60% of their annual base salary to the 401(k) Plan, subject to certain limitations. Beginning in April 2006, the Company began matching in its common stock up to 3% of a participant s base salary. Employer common stock matches vest anywhere from immediately to two years, depending on years of service with the Company. Employees have the ability to transfer funds from the Company stock fund to other plan funds as they choose, subject to blackout periods. The Company issued 14,679 and 12,706 shares of common stock during the years ended December 31, 2008 and 2007, respectively, in connection with matching contributions under the 401(k) Plan.

12. REGULUS THERAPEUTICS

In September 2007, the Company and Isis established Regulus Therapeutics, a company focused on the discovery, development and commercialization of microRNA-based therapeutics, a potential new class of drugs to treat the pathways of human disease. The Company and Isis own 49% and 51%, respectively, of Regulus Therapeutics.

Regulus Therapeutics is operated as an independent company and governed by a managing board comprised of an equal number of directors appointed by each of the Company and Isis. In consideration for the Company s and Isis initial interests in Regulus Therapeutics, each party granted Regulus Therapeutics exclusive licenses to its intellectual property for certain microRNA-based therapeutic applications as well as certain patents in the microRNA field. In addition, the Company made an initial cash contribution to Regulus Therapeutics of $10.0 million, resulting in the Company and Isis making approximately equal aggregate initial capital contributions to Regulus Therapeutics.

In addition, the Company, Isis and Regulus Therapeutics entered into a license and collaboration agreement (the Regulus Therapeutics Collaboration Agreement) to pursue the discovery, development and commercialization of therapeutic products directed to microRNAs. Under the terms of the Regulus Therapeutics Collaboration Agreement, the Company and Isis each assigned to Regulus Therapeutics specified patents and contracts covering microRNA-specific technology. In addition, each of the Company and Isis granted to Regulus Therapeutics an exclusive, worldwide license under its rights to other microRNA-related patents and know-how to develop and commercialize therapeutic products containing compounds that are designed to interfere with or inhibit a particular microRNA, subject to the Company s and Isis existing contractual obligations to third parties. Regulus Therapeutics was also granted the right to request a license from the Company and Isis to develop and commercialize therapeutic products directed to other microRNA compounds, which license is subject to the Company s and Isis approval and to each such party s existing contractual obligations to third parties. Regulus Therapeutics also granted to the Company and Isis an exclusive license to technology developed or acquired by Regulus Therapeutics for use solely within the Company s and Isis respective fields (as defined in the Regulus Therapeutics Collaboration Agreement), but specifically excluding the right to develop, manufacture or commercialize the therapeutic products for which the Company and Isis granted rights to Regulus Therapeutics.

The Regulus Therapeutics Collaboration Agreement ends if, prior to first commercial sale of any product, all development activities cease under the collaboration. The Regulus Therapeutics Collaboration Agreement

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

otherwise expires, on a product-by-product and country-by-country basis, upon the later of expiration of marketing exclusivity for such product or a specified number of years from first commercial sale. If Regulus Therapeutics, the Company or Isis commits an uncured material breach of the Regulus Therapeutics Collaboration Agreement, the Regulus Therapeutics Collaboration Agreement may be terminated with respect to the breaching party or a buy-out may be initiated, depending on the nature of the breach.

In September 2007, the Company also executed a Services Agreement (the Services Agreement) with Isis and Regulus Therapeutics. Under the terms of the Services Agreement, the Company and Isis provide to Regulus Therapeutics, for the benefit of Regulus Therapeutics, certain research and development and general and administrative services for which they are paid by Regulus Therapeutics.

In April 2008, Regulus Therapeutics entered into a worldwide strategic alliance with GlaxoSmithKline (GSK) to discover, develop and commercialize up to four novel microRNA-targeted therapeutics to treat inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. In connection with this alliance, Regulus Therapeutics received $20.0 million in upfront payments from GSK, including a $15.0 million option fee and a loan of $5.0 million evidenced by a promissory note (guaranteed by Isis and the Company) that will convert into Regulus Therapeutics common stock under certain specified circumstances. Regulus Therapeutics could be eligible to receive development, regulatory and sales milestone payments for each of the microRNA-targeted therapeutics discovered and developed as part of the alliance. Regulus Therapeutics would also receive royalty payments on worldwide sales of products resulting from the alliance.

The Company has concluded that Regulus Therapeutics qualifies as a variable interest entity under FASB Interpretation No. 46R, *Consolidation of Variable Interest Entities an interpretation of Accounting Research Bulletin No. 51* (FIN 46R). The LLC Agreement contains transfer restrictions on each of Isis and the Company s LLC interests and, as a result, Isis and the Company are considered related parties under paragraph 16(d)(1) of FIN 46R. The Company has assessed which entity would be considered the primary beneficiary under FIN 46R and has concluded that Isis is the primary beneficiary and, accordingly, the Company has not consolidated Regulus Therapeutics.

The Company accounts for its investment in Regulus Therapeutics using the equity method of accounting. The Company is recognizing the first $10.0 million of losses of Regulus Therapeutics as equity in loss of joint venture (Regulus Therapeutics LLC) in its consolidated statements of operations because the Company is responsible for funding those losses through its initial $10.0 million cash contribution. Thereafter, the Company will recognize 49% of the income and losses of Regulus Therapeutics. Under the equity method, the reimbursement of expenses to the Company is recorded as a reduction to research and development expenses. At December 31, 2008, the Company s investment in the joint venture was $1.6 million, which is recorded as an investment in joint venture (Regulus Therapeutics LLC) in the consolidated balance sheets under the equity method. Summary results of Regulus Therapeutics operations for the years ended December 31, 2008 and 2007 and balance sheets as of December 31, 2008 and 2007 are presented in the table below, in thousands:

	2008	2007
Statement of Operations Data:		

Net revenues	$ 2,111	$ 120
Operating expenses(1)	12,029	1,541
Loss from operations	(9,918)	(1,421)
Other income	256	138
Net loss	$ (9,662)	$ (1,283)
(1) Non-cash stock-based compensation included in operating expenses	$ 2,017	$ 412

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

	2008	2007
Balance Sheet Data:		
Cash	$ 22,411	$ 10,138
Working capital	16,467	9,118
Total assets	23,678	10,446
Notes payable	5,179	
Total stockholders equity	1,745	9,290

Separate financial information for Regulus Therapeutics is included in Exhibit 99.1 to this annual report on Form 10-K.

Regulus Therapeutics, which was initially established as a limited liability company, converted to a C corporation as of January 2, 2009 and changed its name to Regulus Therapeutics Inc. In connection with such conversion, the Company, Isis and Regulus Therapeutics terminated the limited liability company agreement which had previously been in effect.

13. QUARTERLY FINANCIAL DATA (UNAUDITED)

The following information has been derived from unaudited consolidated financial statements that, in the opinion of management, include all recurring adjustments necessary for a fair presentation of such information.

	Three Months Ended			
	March 31, 2008	June 30, 2008	September 30, 2008	December 31, 2008
	(In thousands, except per share data)			
Revenues	$ 22,192	$ 23,833	$ 25,734	$ 24,404
Operating expenses	26,149	36,664	28,968	32,217
Net loss	(1,239)	(12,760)	(2,858)	(9,392)
Net loss per common share basic and diluted	$ (0.03)	$ (0.31)	$ (0.07)	$ (0.23)
Weighted average common shares basic and diluted	40,736	40,908	41,197	41,375

	Three Months Ended			
	March 31, 2007	June 30, 2007	September 30, 2007	December 31, 2007
	(In thousands, except per share data)			
Revenues	$ 7,217	$ 9,133	$ 16,315	$ 18,232
Operating expenses	31,211	24,086	67,653	21,124

Net (loss) income	(21,645)	(12,691)	(52,792)	1,662
Net (loss) income per common share basic and diluted	$ (0.58)	$ (0.34)	$ (1.35)	$ 0.04
Weighted average common shares basic	37,376	37,534	39,025	40,710
Weighted average common shares diluted	37,376	37,534	39,025	42,763

For the three months ended December 31, 2008, the Company discovered that it had understated equity in loss of joint venture by $0.6 million related to non-cash stock-based compensation. To correct its equity in loss of joint venture, the Company recorded a charge of $0.6 million in the three months ended December 31, 2008.

14. SUBSEQUENT EVENT

On January 9, 2009, the Company entered into a license and collaboration agreement (the Cubist Agreement) with Cubist Pharmaceuticals, Inc. (Cubist) to develop and commercialize therapeutic products

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NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

(Licensed Products) based on certain of the Company s RNAi technology for the treatment of RSV. Licensed Products include ALN-RSV01, which is currently in Phase II clinical development for the treatment of RSV infection in adult lung transplant patients, as well as several other second-generation RNAi-based RSV inhibitors, which currently are in pre-clinical studies.

Under the terms of the Cubist Agreement, the Company and Cubist will share responsibility for developing Licensed Products in North America and will each bear one-half of the related development costs. The Company s collaboration with Cubist for the development of Licensed Products in North America will be governed by a joint steering committee comprised of an equal number of representatives from each party. Cubist will have the sole right to commercialize Licensed Products in North America with costs associated with such activities and any resulting profits or losses to be split equally between the Company and Cubist. Throughout the rest of the world (the Royalty Territory), excluding Asia, where the Company has previously partnered its ALN-RSV program with Kyowa Hakko, Cubist will have an exclusive, royalty-bearing license to develop and commercialize Licensed Products.

In consideration for the rights granted to Cubist under the Cubist Agreement, Cubist made a $20.0 million upfront cash payment to the Company. Cubist also has an obligation under the Cubist Agreement to pay the Company milestone payments, totaling up to an aggregate of $82.5 million, upon the achievement of specified development and sales events in the Royalty Territory. In addition, if Licensed Products are successfully developed, Cubist will be required to pay to the company double digit royalties on net sales of Licensed Products in the Royalty Territory, if any, subject to offsets under certain circumstances. Upon achievement of certain development milestones, the Company will have the right to convert the North American co-development and profit sharing arrangement into a royalty-bearing license and, in addition to royalties on net sales in North America, will be entitled to receive additional milestone payments totaling up to an aggregate of $130.0 million upon achievement of specified development and sales events in North America, subject to the timing of the conversion by the Company and the regulatory status of a Licensed Product at the time of conversion. If the Company makes the conversion to a royalty-bearing license with respect to North America, then North America becomes part of the Royalty Territory.

Unless terminated earlier in accordance with the Cubist Agreement, the agreement expires on a country-by-country and Licensed Product-by-Licensed Product basis, (a) with respect to the Royalty Territory, upon the latest to occur of: (1) the expiration of the last-to-expire Company patent covering a Licensed Product, (2) the expiration of the Regulatory-Based Exclusivity Period (as defined in the Cubist Agreement) and (3) ten years from first commercial sale in such country of such License Product by Cubist or its affiliates or sublicensees, and (b) with respect to North America, if the Company has not converted North America into the Royalty Territory, upon the termination of the Cubist Agreement by Cubist upon specified prior written notice. The Company estimates that its fundamental RNAi patents covered under the Agreement will expire both in and outside of the United States generally between 2016 and 2025. Allowed claims covering ALN-RSV01 in the United States would expire in 2026. These patent rights are subject to any potential patent term extensions and/or supplemental protection certificates extending such term extensions in countries where such extensions may become available. In addition, more patent filings relating to the collaboration may be made in the future. Cubist has the right to terminate the Cubist Agreement at any time (1) upon three months prior written notice if such notice is given prior to the acceptance for filing of the first application for regulatory approval of a Licensed Product or (2) upon nine months prior written notice if such notice is given after the acceptance for filing of the first application for regulatory approval. Either party may terminate the Cubist Agreement in the event the other party fails to cure a material breach or upon patent-related challenges by the other party.

During the term of the Cubist Agreement, neither party nor its affiliates may develop, manufacture or commercialize anywhere in the world, outside of Asia, a therapeutic or prophylactic product that specifically targets RSV, except for Licensed Products developed, manufactured or commercialized pursuant to the Cubist Agreement.

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Our management, with the participation of our chief executive officer and vice president of finance and treasurer, evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2008. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2008, the Company s chief executive officer and vice president of finance and treasurer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management s report on our internal control over financial reporting (as defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) and the independent registered public accounting firm s report on the effectiveness of our internal control over financial reporting are included in Item 8 of this annual report on Form 10-K and are incorporated herein by reference.

No change in our internal control over financial reporting occurred during the fiscal quarter ended December 31, 2008 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

ITEM 9B. OTHER INFORMATION

None.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

We will file with the SEC a definitive Proxy Statement, which we refer to herein as the Proxy Statement, not later than 120 days after the close of the fiscal year ended December 31, 2008. The information required by this item is incorporated herein by reference to the information contained under the sections captioned Proposal One Election of Class I Directors, Section 16(a) Beneficial Ownership Reporting Compliance and Corporate Governance of the Proxy Statement. The information required by this item relating to executive officers is included in Part I, Item 1 Business-Executive Officers of the Registrant of this annual report on Form 10-K.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Information about Executive Officer and Director Compensation, Compensation Committee Interlocks and Insider Participation , Employment Arrangements and Compensation Committee Report of the Proxy Statement.

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ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Security Ownership of Certain Beneficial Owners and Management Information about Executive Officer and Director Compensation and Securities Authorized for Issuance Under Equity Compensation Plans of the Proxy Statement.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Corporate Governance, Employment Arrangements and Certain Relationships and Related Transactions of the Proxy Statement.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this item is incorporated herein by reference to the information contained under the sections captioned Corporate Governance, Principal Accountant Fees and Services and Pre-Approval Policies and Procedures of the Proxy Statement.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) (1) Financial Statements

The following consolidated financial statements are filed as part of this report under Item 8 Financial Statements and Supplementary Data :

(a) (2) List of Schedules

All schedules to the consolidated financial statements are omitted as the required information is either inapplicable or presented in the consolidated financial statements.

(a) (3) List of Exhibits

The exhibits which are filed with this report or which are incorporated herein by reference are set forth in the Exhibit Index hereto.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized, on March 2, 2009.

ALNYLAM PHARMACEUTICALS, INC.

By: /s/ John M. Maraganore, Ph.D.

John M. Maraganore, Ph.D.
Chief Executive Officer

Pursuant to the requirements of the Securities Exchange Act of 1934, the Report has been signed below by the following persons on behalf of the Registrant and in the capacities indicated as of March 2, 2009.

Name	Title
/s/ John M. Maraganore, Ph.D.	Director and Chief Executive Officer (Principal Executive Officer)
John M. Maraganore, Ph.D.	
/s/ Patricia L. Allen	Vice President of Finance and Treasurer (Principal Financial and Accounting Officer)
Patricia L. Allen	
/s/ John K. Clarke	Director
John K. Clarke	
/s/ Victor J. Dzau, M.D.	Director
Victor J. Dzau, M.D.	
/s/ Vicki L. Sato, Ph.D.	Director
Vicki L. Sato, Ph.D.	
/s/ Paul R. Schimmel, Ph.D.	Director
Paul R. Schimmel, Ph.D.	
/s/ Edward M. Scolnick, M.D.	Director
Edward M. Scolnick, M.D.	
/s/ Phillip A. Sharp, Ph.D.	Director

Phillip A. Sharp, Ph.D.

/s/ Kevin P. Starr	Director
Kevin P. Starr	
/s/ James L. Vincent	Director
James L. Vincent	

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EXHIBIT INDEX

Exhibit No.	Exhibit
3.1	Restated Certificate of Incorporation of the Registrant (filed as Exhibit 3.1 to the Registrant s Quarterly Report on Form 10-Q filed on August 11, 2005 (File No. 000-50743) for the quarterly period ended June 30, 2005 and incorporated herein by reference)
3.2	Amended and Restated Bylaws of the Registrant (filed as Exhibit 3.4 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
4.1	Specimen certificate evidencing shares of common stock (filed as Exhibit 4.1 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
4.2	Rights Agreement dated as of July 13, 2005 between the Registrant and EquiServe Trust Company, N.A., as Rights Agent, which includes as Exhibit A the Form of Certificate of Designations of Series A Junior Participating Preferred Stock, as Exhibit B the Form of Rights Certificate and as Exhibit C the Summary of Rights to Purchase Preferred Stock (filed as Exhibit 4.1 to the Registrant s Current Report on Form 8-K filed on July 14, 2005 (File No. 000-50743) and incorporated herein by reference)
10.1*	2002 Employee, Director and Consultant Stock Plan, as amended, together with forms of Incentive Stock Option Agreement, Non-qualified Stock Option Agreement and Restricted Stock Agreement (filed as Exhibit 10.1 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.2*	2003 Employee, Director and Consultant Stock Plan, as amended, together with forms of Incentive Stock Option Agreement, Non-qualified Stock Option Agreement and Restricted Stock Agreement (filed as Exhibit 10.2 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.3*	2004 Stock Incentive Plan, as amended (filed as Exhibit 10.3 to the Registrant s Annual Report on Form 10-K filed on March 7, 2008 (File No. 000-50743) for the annual period ended December 31, 2007 and incorporated herein by reference)
10.4*	Forms of Incentive Stock Option Agreement and Nonstatutory Stock Option Agreement under 2004 Stock Incentive Plan, as amended (filed as Exhibit 10.3 to the Registrant s Quarterly Report on Form 10-Q filed on August 11, 2005 (File No. 000-50743) for the quarterly period ended June 30, 2005 and incorporated herein by reference)
10.5*	Form of Nonstatutory Stock Option Agreement under 2004 Stock Incentive Plan granted to John M. Maraganore, Ph.D., on December 21, 2004 (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on December 28, 2004 (File No. 000-50743) and incorporated herein by reference)
10.6*	Form of Nonstatutory Stock Option Agreement under 2004 Stock Incentive Plan granted to James L. Vincent on July 12, 2005 (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on July 13, 2005 (File No. 000-50743) and incorporated herein by reference)
10.7*	Form of Restricted Stock Agreement under 2004 Stock Incentive Plan issued to James L. Vincent on July 12, 2005 (filed as Exhibit 10.2 to the Registrant s Current Report on Form 8-K filed on July 13, 2005 (File No. 000-50743) and incorporated herein by reference)
10.8*	2004 Employee Stock Purchase Plan, as amended (filed as Exhibit 10.8 to the Registrant s Annual Report on Form 10-K filed on March 7, 2008 (File No. 000-50743) for the annual period ended December 31, 2007 and incorporated herein by reference)
10.9	Investor Rights Agreement entered into as of March 11, 2004 by and between the Registrant and Isis Pharmaceuticals, Inc. (filed as Exhibit 10.25 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.10	

	Stock Purchase Agreement, dated as of September 6, 2005, by and between the Registrant and Novartis Pharma AG (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on September 12, 2005 (File No. 000-50743) and incorporated herein by reference)
10.11	Investor Rights Agreement, dated as of September 6, 2005, by and between the Registrant. and Novartis Pharma AG (filed as Exhibit 10.2 to the Registrant s Current Report on Form 8-K filed on September 12, 2005 (File No. 000-50743) and incorporated herein by reference)

Exhibit No.	Exhibit
10.12*	Letter Agreement between the Registrant and John M. Maraganore, Ph.D. dated October 30, 2002 (filed as Exhibit 10.7 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.13*	Letter Agreement between the Registrant and Barry E. Greene dated September 29, 2003 (filed as Exhibit 10.10 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.14	Lease, dated as of September 26, 2003 by and between the Registrant and Three Hundred Third Street LLC (filed as Exhibit 10.15 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.15	License Agreement between Cancer Research Technology Limited and Alnylam U.S., Inc. dated July 18, 2003 (filed as Exhibit 10.16 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.16	License Agreement between the Carnegie Institution of Washington and Alnylam Europe, AG, effective March 1, 2002, as amended by letter agreements dated September 2, 2002 and October 28, 2003 (filed as Exhibit 10.17 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.17	License Agreement by and between the Cold Spring Harbor Laboratory and Alnylam U.S., Inc. dated December 30, 2003 (filed as Exhibit 10.18 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.18	Co-exclusive License Agreement between Garching Innovation GmbH (now known as Max Planck Innovation GmbH) and Alnylam U.S., Inc. dated December 20, 2002, as amended by Amendment dated July 8, 2003 together with Indemnification Agreement by and between Garching Innovation GmbH (now known as Max Planck Innovation GmbH) and Alnylam Pharmaceuticals, Inc. effective April 1, 2004 (filed as Exhibit 10.19 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.19	Co-exclusive License Agreement between Garching Innovation GmbH (now known as Max Planck Innovation GmbH) and Alnylam Europe, AG dated July 30, 2003 (filed as Exhibit 10.20 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.20	Agreement between the Registrant, Garching Innovation GmbH (now known as Max Planck Innovation GmbH), Alnylam U.S., Inc. and Alnylam Europe AG dated June 14, 2005 (filed as Exhibit 10.8 to the Registrant s Quarterly Report on Form 10-Q filed on August 11, 2005 (File No. 000-50743) for the quarterly period ended June 30, 2005 and incorporated herein by reference)
10.21	Agreement between The Board of Trustees of the Leland Stanford Junior University and Alnylam U.S., Inc. effective as of September 17, 2003 (filed as Exhibit 10.21 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.22	Strategic Collaboration and License Agreement effective as of March 11, 2004 between Isis Pharmaceuticals, Inc. and the Registrant (filed as Exhibit 10.24 to the Registrant s Registration Statement on Form S-1 (File No. 333-113162) and incorporated herein by reference)
10.23 #	Research Collaboration and License Agreement effective as of October 12, 2005 by and between the Registrant and Novartis Institutes for BioMedical Research, Inc. (previously filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on October 12, 2005 (File No. 000-50743))
10.24	First Amendment to Lease, dated March 16, 2006, by and between the Registrant and ARE-MA Region No. 28, LLC (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on March 17, 2006 (File No. 000-50743) and incorporated herein by reference)

10.25	Collaboration and License Agreement dated September 20, 2006, by and between the Registrant and Biogen Idec Inc. (filed as Exhibit 10.1 to the Registrant s Quarterly Report on Form 10-Q filed on November 9, 2006 (File No. 000-50743) for the quarterly period ended September 30, 2006 and incorporated herein by reference)

Exhibit No.	Exhibit
10.26 #	License and Collaboration Agreement, entered into as of July 8, 2007, by and among F. Hoffmann-La Roche, Ltd, Hoffman-La Roche Inc., the Registrant and, for limited purposes, Alnylam Europe AG (previously filed as Exhibit 10.1 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007)
10.27	Common Stock Purchase Agreement dated as of July 8, 2007 between the Registrant and Roche Finance Ltd (filed as Exhibit 10.2 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.28	Share Purchase Agreement, dated as of July 8, 2007, among Alnylam Europe AG, the Registrant and Roche Pharmaceuticals GmbH (filed as Exhibit 10.3 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.29	Amended and Restated Collaboration Agreement, entered into as of July 27, 2007, by and between the Registrant and Medtronic, Inc. (filed as Exhibit 10.4 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.30	License and Collaboration Agreement, entered into as of September 6, 2007, by and among the Registrant, Isis Pharmaceuticals, Inc. and Regulus Therapeutics LLC (filed as Exhibit 10.5 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.31	Termination Agreement, dated as of September 18, 2007, by and between Merck & Co., Inc. and the Registrant (filed as Exhibit 10.7 to the Registrant s Quarterly Report on Form 10-Q filed on November 8, 2007 (File No. 000-50743) for the quarterly period ended September 30, 2007 and incorporated herein by reference)
10.32	License and Collaboration Agreement entered into as of May 27, 2008 by and among Takeda Pharmaceutical Company Limited and the Registrant (filed as Exhibit 10.1 to the Registrant s Quarterly Report on Form 10-Q filed on August 8, 2008 (File No. 000-50743) for the quarterly period ended June 30, 2008 and incorporated herein by reference)
21.1#	Subsidiaries of the Registrant
23.1#	Consent of PricewaterhouseCoopers LLP, Independent Registered Public Accounting Firm
23.2#	Consent of Ernst & Young LLP, Independent Auditors of Regulus Therapeutics LLC
31.1#	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002, Rule 13(a)- 14(a)/15d-14(a), by Chief Executive Officer
31.2#	Certification pursuant to Section 302 of the Sarbanes-Oxley Act of 2002, Rule 13(a)- 14(a)/15d-14(a), by Vice President of Finance and Treasurer
32.1#	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Chief Executive Officer
32.2#	Certification pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, by Vice President of Finance and Treasurer
99.1#	Regulus Therapeutics LLC Financial Statements

* Management contracts or compensatory plans or arrangements required to be filed as an exhibit hereto pursuant to Item 15(a) of Form 10-K.

Indicates confidential treatment requested as to certain portions, which portions were omitted and filed separately with the Securities and Exchange Commission pursuant to a Confidential Treatment Request.

\# Filed herewith. The Registrant is refiling Exhibits 10.23 and 10.26, which include portions previously omitted pursuant to Confidential Treatment Requests.