ALNYLAM PHARMACEUTICALS, INC.
Form 10-Q
November 08, 2007

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

FORM 10-Q

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

For the quarterly period ended September 30, 2007

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 000-50743

ALNYLAM PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	77-0602661
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
300 Third Street, Cambridge, MA	02142
(Address of principal executive offices)	(Zip Code)

(617) 551-8200

(Registrant s telephone number, including area code)

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

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

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

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

As of October 31, 2007, the registrant had 40,699,884 shares of Common Stock, $0.01 par value per share, outstanding.

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ALNYLAM PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)
(Unaudited)

	September 30, 2007	December 31, 2006
ASSETS		
Current assets:		
Cash and cash equivalents	$ 200,547	$ 127,955
Marketable securities	267,831	89,305
Collaboration receivables	5,129	3,829
Prepaid expenses and other current assets	4,125	1,695
Total current assets	477,632	222,784
Property and equipment, net	10,434	12,173
Intangible assets, net	1,610	1,933
Restricted cash	5,313	2,313
Other assets	201	803
Investment in joint venture (Regulus Therapeutics LLC)	9,901	
Total assets	$ 505,091	$ 240,006
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 7,057	$ 4,085
Accrued expenses	11,746	4,479
Income taxes payable	3,296	
Current portion of notes payable	3,705	3,217
Deferred revenue	61,652	11,144
Total current liabilities	87,456	22,925
Deferred revenue, net of current portion	217,051	6,786
Deferred rent	3,120	3,202
Notes payable, net of current portion	3,946	5,919
Other long-term liabilities	583	
Total liabilities	312,156	38,832
Commitments and contingencies		
Stockholders equity:		
Preferred stock, $0.01 par value, 5,000,000 shares authorized and no shares issued and outstanding at September 30, 2007 and December 31, 2006		
Common stock, $0.01 par value, 125,000,000 shares authorized; 40,612,545 and 37,050,631 shares issued and outstanding at September 30, 2007 and December 31, 2006, respectively	406	371

Additional paid-in capital	420,039	340,779
Deferred stock compensation		(89)
Accumulated other comprehensive income	145	640
Accumulated deficit	(227,655)	(140,527)
Total stockholders equity	192,935	201,174
Total liabilities and stockholders equity	$ 505,091	$ 240,006

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

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ALNYLAM PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except per share amounts)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2007	2006	2007	2006
Net revenues from research collaborators	$ 16,315	$ 8,211	$ 32,665	$ 19,949
Operating expenses:				
Research and development [1]	59,618	12,697	105,102	37,003
General and administrative [1]	8,035	4,118	17,848	12,456
Total operating expenses	67,653	16,815	122,950	49,459
Loss from operations	(51,338)	(8,604)	(90,285)	(29,510)
Other income (expense):				
Equity in loss of joint venture (Regulus Therapeutics LLC)	(139)		(139)	
Interest income	4,311	1,555	9,579	4,353
Interest expense	(272)	(265)	(833)	(733)
Other expense	(169)	(86)	(265)	(280)
Total other income, net	3,731	1,204	8,342	3,340
Loss before income taxes	(47,607)	(7,400)	(81,943)	(26,170)
Provision for income taxes	(5,185)		(5,185)	
Net loss	$ (52,792)	$ (7,400)	$ (87,128)	$ (26,170)
Net loss per common share basic and diluted	$ (1.35)	$ (0.23)	$ (2.29)	$ (0.83)
Weighted average common shares basic and diluted	39,025	32,122	37,984	31,465
Comprehensive loss:				
Net loss	$ (52,792)	$ (7,400)	$ (87,128)	$ (26,170)

Foreign currency translation adjustments	(687)	47	(605)	276
Unrealized gain on marketable securities	273	104	108	129
Comprehensive loss	$ (53,206)	$ (7,249)	$ (87,625)	$ (25,765)

(1) Non-cash stock-based compensation expense included in these amounts are as follows:

Research and development	$ 5,667	$ 883	$ 7,687	$ 3,331
General and administrative	2,255	831	4,181	2,364

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

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ALNYLAM PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)
(Unaudited)

	Nine Months Ended September 30,	
	2007	**2006**
Cash flows from operating activities:		
Net loss	$ (87,128)	$ (26,170)
Adjustments to reconcile net income (loss) to net cash used in operating activities:		
Depreciation and amortization	3,180	2,868
Deferred income tax provision	1,889	
Non-cash stock-based compensation	11,868	5,695
Non-cash license expense	7,909	130
Charge for 401(k) company stock match	204	91
Equity in loss of joint venture (Regulus Therapeutics LLC)	139	
Changes in operating assets and liabilities:		
Proceeds from landlord for tenant improvements	295	1,106
Collaboration receivables	(1,292)	(4,238)
Prepaid expenses and other assets	(5,546)	102
Accounts payable	2,968	469
Income taxes payable	3,296	
Accrued expenses	7,139	1,252
Deferred revenue	260,118	(1,435)
Deferred rent	(82)	113
Net cash provided by (used in) operating activities	204,957	(20,017)
Cash flows from investing activities:		
Purchases of property and equipment	(3,554)	(4,695)
Disposals of property and equipment	2,343	
Purchases of marketable securities	(356,264)	(118,798)
Sales of marketable securities	177,738	98,286
Investment in joint venture (Regulus Therapeutics LLC)	(10,000)	
Net cash used in investing activities	(189,737)	(25,207)
Cash flows from financing activities:		
Proceeds from issuance of common stock, net of issuance costs	59,364	62,847
Proceeds from notes payable	957	3,613
Repayments of notes payable	(2,441)	(1,525)
Net cash provided by financing activities	57,880	64,935
Effect of exchange rate on cash	(508)	48

Net increase in cash and cash equivalents	72,592	19,759
Cash and cash equivalents, beginning of period	127,955	15,757
Cash and cash equivalents, end of period	$ 200,547	$ 35,516

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

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ALNYLAM PHARMACEUTICALS, INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
(Unaudited)

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Principles of Consolidation

The accompanying condensed consolidated financial statements of Alnylam Pharmaceuticals, Inc. (the Company or Alnylam) are unaudited and have been prepared in accordance with accounting principles generally accepted in the United States applicable to interim periods and, in the opinion of management, include all normal and recurring adjustments that are necessary to present fairly the results of operations for the reported periods. The Company s condensed consolidated financial statements have also been prepared on a basis substantially consistent with, and should be read in conjunction with, the Company s audited consolidated financial statements for the year ended December 31, 2006, which were filed in the Company s Annual Report on Form 10-K with the Securities and Exchange Commission (the SEC) on March 12, 2007. The results of the Company s operations for any interim period are not necessarily indicative of the results of the Company s operations for any other interim period or for a full fiscal year.

The accompanying condensed consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiaries Alnylam U.S., Inc., Alnylam Europe AG (Alnylam Europe) and Alnylam Securities Corporation. All significant intercompany accounts and transactions have been eliminated.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States 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 financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Reclassifications

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

Net Income (Loss) Per Common Share

The Company accounts for and discloses net income (loss) per common share in accordance with Statement of Financial Accounting Standard (SFAS) No. 128, *Earnings per Share.* Basic net income (loss) per common share is computed by dividing net income (loss) attributable to common stockholders by the weighted average number of common shares outstanding. Diluted net income (loss) per common share is computed by dividing net income (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 and warrants (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 share is the same as basic net loss per share.

The following table sets forth the potential common shares excluded from the calculation of net loss per share because their inclusion would be anti-dilutive (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2007	2006	2007	2006
Options to purchase common stock	4,017	3,945	4,017	3,945
Unvested restricted common stock	57		57	
Options that were exercised before vesting	8	36	14	44
	4,082	3,981	4,088	3,989

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Recent Accounting Pronouncements

In September 2006, the Financial Accounting Standard Board (FASB) issued SFAS No. 157, *Fair Value Measurements,* 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. The standard is expected to be effective for financial statements for fiscal years beginning after November 15, 2007. This standard formalizes the measurement principles to be utilized in determining fair value for purposes such as derivative valuation and impairment analysis. The Company is evaluating the implications of this standard, but currently, does not expect it to have a significant impact on its consolidated financial statements.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities-including an amendment of SFAS 115* (SFAS No. 159). The new statement allows entities to choose, at specified election dates, to measure at fair value eligible financial assets and liabilities that are not otherwise required to be measured at fair value. If a company elects the fair value option for an eligible item, changes in that item s fair value in subsequent reporting periods must be recognized in current earnings. SFAS No. 159 is effective for fiscal years beginning after November 15, 2007. The Company is currently evaluating the potential impact of SFAS No. 159 on its consolidated financial statements.

In June 2007, the FASB reached a consensus on Emerging Issues Task Force (EITF) Issue No. 07-03, *Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development Activities* (EITF 07-03). EITF 07-03 requires companies to defer and capitalize, until the goods have been delivered or the related services have been rendered, non-refundable advance payments for goods that will be used or services that will be performed in future research and development activities. EITF 07-03 is effective for fiscal years beginning after December 15, 2007. The Company does not expect EITF 07-03 will have a material impact on its consolidated financial statements.

2. NOTES PAYABLE

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 allows the Company to draw down amounts under the line of credit through December 31, 2007 upon adherence to certain conditions. All borrowings under this line of credit are collateralized by the assets financed and the agreement contains certain provisions that restrict the Company s ability to dispose of or transfer these assets. During 2006, the Company borrowed an aggregate of $4.2 million from Oxford pursuant to the agreement. Of such amount, $1.3 million bears interest at fixed rates ranging from 10.1% to 10.4% and is being repaid in 48 monthly installments of principal and interest. The remainder of such amount, $2.9 million, bears interest at fixed rates ranging from 10.0% to 10.4% and is being repaid in 36 monthly installments of principal and interest. In May 2007, the Company borrowed an aggregate of $1.0 million from Oxford pursuant to the agreement. Of such amount, $0.6 million bears interest at a fixed rate of 10% and is being repaid in 48 monthly installments of principal and interest. The remainder of such amount, $0.4 million, bears interest at a fixed rate of 10% and is being repaid in 36 monthly installments of principal and interest. As of September 30, 2007, there was $3.7 million outstanding under this line of credit with Oxford.

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. All borrowings under the line of credit are collateralized by the assets financed and the agreement contains certain provisions that restrict the Company s ability to dispose of or transfer these assets. The outstanding principal bears interest at a fixed rate of 9.25%, except for the drawdown made in December 2005, which bears interest at a fixed rate of 10.25%. The outstanding principal matures at various dates through December 2009. On the maturity of each equipment advance under the line of credit, the Company is required to pay, in addition to the principal and interest due, an additional amount of 11.5% of the original principal. This amount is being accrued over the applicable borrowing period as additional interest expense. As of September 30, 2007, there was $4.0 million outstanding under this line of credit with Lighthouse.

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At September 30, 2007, future cash payments under the notes payable to Lighthouse and Oxford, including interest, were as follows, in thousands:

Remainder of 2007	$ 1,067
2008	4,268
2009	3,513
2010	480
2011	79
Total through 2011	9,407
Less: portion representing interest	1,756
Principal	7,651
Less: current portion	3,705
Long-term notes payable	$ 3,946

3. SIGNIFICANT AGREEMENTS

Roche

In July 2007, the Company and, for limited purposes, Alnylam Europe, entered into a License and Collaboration Agreement (the LCA) with F. Hoffmann-La Roche Ltd (Roche Basel), and Hoffman-La Roche Inc. (together with Roche Basel, Roche). The LCA, which became effective in August 2007, provides for the grant to Roche of a non-exclusive license to the Company s intellectual property to develop and commercialize therapeutic products that function through RNA interference (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 other therapeutic areas under certain circumstances.

In consideration for the rights granted to Roche under the LCA, Roche paid the Company $273.5 million in upfront cash payments. Roche is also required to make payments to the Company upon achievement of specified development and sales milestones set forth in the LCA and royalty payments based on worldwide annual net sales, if any, of RNAi therapeutic products by Roche, its affiliates and sublicensees.

Under the LCA, the Company and Roche have 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.

The term of the LCA generally ends upon the later of expiration of the last-to-expire patent covering a licensed product and ten years from first commercial sale of 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 to the Company, 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 twelve months. The LCA may also be terminated by either party in the event that 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.

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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 Basel and Roche Finance (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 includes transition services to be performed by Roche Kulmbach employees at various levels through August 2008. The Company will reimburse Roche for these services at an agreed-upon rate. The Company is recording these services as contra revenue (a reduction of revenues) in the period incurred. 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 compensation expense during the three months ended September 30, 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 has initially recorded $278.5 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 $1.2 million.

When evaluating multiple element arrangements, the Company considers whether the components of the arrangement represent separate units of accounting as defined in EITF Issue No. 00-21, *Revenue Arrangements with Multiple Deliverables* (EITF 00-21). Application of this standard requires subjective determinations and requires management to make judgments about the value of each individual element and whether it is separable from the other aspects of the contractual relationship. 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 services, 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 milestones are achieved, and to the extent they are within the five year term, the amounts will be recognized as revenue prospectively over the remaining period of performance.

In connection with the LCA and the Common Stock Purchase Agreement, the Company incurred $27.5 million of license fees payable to the Company s licensors, primarily Isis Pharmaceuticals, Inc. (Isis), during the quarter ended September 30, 2007, in accordance with the applicable license agreements with those parties.

Novartis Broad Alliance

Beginning in September 2005, the Company entered into a series of transactions with Novartis Pharma AG and its affiliate Novartis Institute for Biomedical Research (collectively, 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).

Under the terms of the Stock Purchase Agreement, Novartis purchased 5,267,865 shares of the Company s common stock for an aggregate purchase price of $58.5 million, which represented approximately 13% of the Company s outstanding common stock at September 30, 2007.

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Under the terms of the Collaboration and License Agreement, the parties agreed to 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. The Collaboration and License Agreement has an initial term of three years and may be extended for two additional one-year terms at the election of Novartis. Novartis made upfront payments totaling $10.0 million to the Company in October 2005 and is required to provide the Company with research funding and milestone payments as well as royalties on annual net sales of products, if any, resulting from the Collaboration and License Agreement. The Collaboration and License Agreement also provides Novartis with a non-exclusive option to integrate the Company s intellectual property relating to certain RNAi technology into Novartis operations under certain circumstances (the Integration Option). In connection with the exercise of the Integration Option, Novartis will be required to make certain additional payments to the Company.

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 by Novartis. These payments, in addition to research funding and certain milestone payments under the Novartis Agreements, are recognized as revenue using the proportional performance method over the estimated duration of the Novartis Agreements of ten years. Under this model, the revenue recognized by the Company is limited to the amount of non-refundable payments received or receivable to date. Quarterly, the Company updates its estimates of effort remaining to complete its obligations under the agreements, the expected term of the agreements and the expected total revenues based on all information known that could affect the Company s estimates.

Novartis Pandemic Flu Alliance

In February 2006, the Company entered into an alliance with Novartis for the development of RNAi therapeutics for pandemic flu (the Novartis Flu Agreement). The Novartis Flu Agreement supplements and, to the extent described therein, supersedes in relevant part the Collaboration and License Agreement for the broad Novartis alliance. Under the terms of the Novartis Flu Agreement, the Company and Novartis have joint responsibility for development of RNAi therapeutics for pandemic flu and Novartis provides funding for the research performed by the Company. Novartis will have primary responsibility for commercialization of such RNAi therapeutics worldwide, but the Company will be actively involved, and may in certain circumstances take the lead, in commercialization in the United States. The Company is eligible to receive significant funding from Novartis for its efforts on RNAi therapeutics for pandemic flu, and to receive a significant share of any profits.

Biogen Idec

In September 2006, the Company entered into a Collaboration and License Agreement (the Biogen Idec Collaboration Agreement) with Biogen Idec, Inc. (Biogen Idec). The collaboration is focused on the discovery and development of therapeutics based on RNAi for the potential treatment of progressive multifocal leukoencephalopathy (PML). The Company and Biogen Idec are initially conducting investigative research into the potential of RNAi technology to develop therapeutics to treat 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 also received an upfront $5.0 million payment from Biogen Idec. The Company is recognizing the remaining deferred revenue using a proportional performance model over the period of expected performance of five years. In addition, assuming the successful development and utilization of a product resulting from the collaboration, Biogen Idec will be required to pay the Company milestone and royalty payments.

Medtronic

In July 2007, the Company and Medtronic, Inc. (Medtronic) entered into an amended and restated collaboration agreement (the Amended and Restated Collaboration Agreement) 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 (the Initial Collaboration Agreement), 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, the Company and Medtronic will continue their existing development program focused on developing a combination drug-device product for the treatment of Huntington s disease. In addition, as provided for in the Initial Collaboration Agreement, the companies 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 small

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interfering RNAs (siRNAs) discovered and developed using the Company s RNAi therapeutics platform to the human nervous system through implantable infusion devices developed by Medtronic. The Company 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, the parties will each fund 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 the Company based on net sales of any such products, which royalties in the United States are designed to approximate 50% of the profit associated with the sale of such product and which in Europe, similar to more traditional pharmaceutical royalties, 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.

Unlike the Initial Collaboration Agreement, the Amended and Restated Collaboration Agreement does not require Medtronic to make any equity investment in the Company.

The Amended and Restated Collaboration Agreement expires, on a product-by-product and country-by-country basis, upon expiration of the royalty term for the applicable product. The royalty term is the longer of a specified number of years from the first commercial sale of the applicable product and the expiration of the last-to-expire of specified patent rights. Royalties are paid at a lower level during any part of a royalty term in which specified patent coverage does not exist. Either party may terminate the Amended and Restated Collaboration Agreement on 60 days prior written notice if the other party materially breaches the agreement in specified ways and fails to cure the breach within the 60-day notice period. Either party may also terminate the agreement in the event that specified pre-clinical testing does not yield results meeting specified success criteria.

NIH Contract

In September 2006, the Company was awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever viruses, including the Ebola virus, with the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH). The federal contract is expected to provide the Company with up to $23.0 million in funding over a four-year period to develop RNAi therapeutics as anti-viral drugs targeting 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 has committed to pay the Company up to $14.2 million over the first two years of the contract and, subject to the progress of the program and budgetary considerations in future years, the remaining $8.8 million over the last two years of the contract.

Department of Defense Contract

In August 2007, the Company was awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus with the United States Department of Defense. The federal contract is expected to provide the Company with up to $38.6 million in funding through the second quarter of 2010 to develop RNAi therapeutics for hemorrhagic fever virus infection. Viral hemorrhagic fevers are considered by federal agencies to be high priority agents that pose a potential risk to national security because they can be easily transmitted from person to person, result in high mortality rates and require special action for public health preparedness. This contract is with the Defense Threat Reduction Agency 2007 Medical Science and Technology Chemical and Biological Defense Transformational Medical Technologies Initiative, the mission of which is to provide state-of-the-art defense capabilities to United States military personnel by addressing traditional and non-traditional biological threats. Of the $38.6 million in funding, the government has committed to pay the Company up to $7.2 million through April 2008 and, subject to the progress of the program and budgetary considerations in future years, the remaining $31.4 million over the last two years of the contract.

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Merck

In July 2006, the Company executed an Amended and Restated Research Collaboration and License Agreement (the Amended License Agreement) with Merck & Co., Inc. (Merck), which amended and restated the Research Collaboration and License Agreement, dated September 8, 2003, between the Company and Merck, as amended (the Original License Agreement). Under the Amended License Agreement, the collaboration between the Company and Merck focused on developing RNAi therapeutics for targets associated with human diseases, and the parties collaborated on a program directed to the NOGO pathway, along with two other joint development programs selected by the Company and co-funded by Merck.

In September 2007, the Company 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. As a result of the Termination Agreement, the Company recognized $3.5 million of revenue during the three months ended September 30, 2007, representing the remaining deferred revenue under the Amended License Agreement.

4. 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. The Company expensed $7.3 million and $16.9 million related to these agreements during the three and nine months ended September 30, 2007, respectively. In connection with one such agreement with Tekmira Pharmaceuticals Corporation, the Company issued 361,990 shares of common stock in a private placement in January 2007, valued at $7.9 million, which amount is included in the amount expensed during the nine months ended September 30, 2007.

5. INCOME TAXES

The Company adopted the provisions of FASB Interpretation No. 48 (FIN 48) on January 1, 2007, *Accounting for Uncertainty in Income Taxes an interpretation of FASB Statement 109,* 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 fully recognize 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 September 30, 2007, the Company did not have any unrecognized tax benefits.

At December 31, 2006, the Company had federal and state net operating loss (NOL) carryforwards of $54.4 million and $53.6 million available, respectively, to reduce future taxable income and which will expire at various dates beginning in 2008 through 2026. At December 31, 2006, federal and state research and development and other credit carryforwards were $1.8 million and $1.0 million, respectively, available to reduce future tax liabilities, and, which will expire at various dates beginning in 2018 through 2026. Utilization of the NOL and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that have occurred previously or that could occur in the future provided by Section 382 of the Internal Revenue Code of 1986, as amended (the Code) as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an ownership change, as defined by Section 382 of the Code, results from transactions increasing the ownership of certain shareholders or public groups in the stock of a corporation by more than 50 percentage points over a three-year period. Since the Company s formation, the Company has raised capital through the issuance of capital stock on several occasions (both pre and post initial public offering) which, combined with the purchasing stockholders subsequent disposition of those shares, may have resulted in a change of control, as defined by Section 382 of the Code, or could result in a change of control in the future upon subsequent disposition. The Company has substantially completed its assessment of the impact of a change of control on its NOL carryforwards and the amount of usable research and development credits and does not

expect to have any material limitation that would result in expiration of a portion of the NOL or research and development credit carryforwards before utilization.

Through June 30, 2007, the Company has always generated operating losses and, as a result, had not recorded a tax provision and recorded a full valuation allowance against its net deferred tax assets. The proceeds from the sale of the Company s German operations to Roche Kulmbach generated an income tax provision of $5.2 million for the three months ended September 30, 2007 and a related foreign tax liability of $3.3 million as of September 30, 2007, which is expected to be paid in early 2008. The proceeds from

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the Roche alliance are expected to create a federal and state tax liability for the Company in 2008, along with generating additional deferred tax assets related to the amount of the revenue that is deferred for financial reporting purposes. The Company will recognize a deferred tax asset in 2008 to the extent that the asset can be realized to offset this expected current tax liability. At December 31, 2006, the valuation allowance was $50.9 million.

6. INVESTMENT IN JOINT VENTURE (REGULUS THERAPEUTICS LLC)

In September 2007, the Company entered into a joint venture with Isis to create a new Delaware limited liability company, Regulus Therapeutics LLC (Regulus Therapeutics), to focus on the discovery, development and commercialization of microRNA (miRNA) 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.

Under the terms of the Limited Liability Agreement among the Company, Isis and Regulus Therapeutics (the LLC Agreement), Regulus Therapeutics will be 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 agreed to grant Regulus Therapeutics exclusive licenses to its intellectual property for certain miRNA therapeutic applications as well as certain patents in the miRNA field. In addition, the Company agreed to make 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 connection with the execution of the LLC Agreement, 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 miRNAs. Under the terms of the Regulus Therapeutics Collaboration Agreement, the Company and Isis each assigned to Regulus Therapeutics specified patents and contracts covering miRNA therapeutic-specific technology. In addition, each of the Company and Isis granted to Regulus Therapeutics an exclusive, worldwide license under its rights to other miRNA therapeutic-related patents and know-how to develop and commercialize therapeutic products containing compounds that are designed to interfere with or inhibit a particular miRNA, 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 miRNA 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 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 under the LLC Agreement, depending on the nature of the breach.

In connection with the execution of the LLC Agreement and Regulus Therapeutics Collaboration Agreement, 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 agreed to provide to Regulus Therapeutics, for the benefit of Regulus Therapeutics, certain research and development and general and administrative services, as set forth in an operating plan mutually agreed upon by the Company and Isis. The Services Agreement provides that the Company and Isis generally will be paid by Regulus Therapeutics for services. Subject to certain exceptions, the Services Agreement will terminate upon the termination or expiration of the LLC Agreement or the Regulus Therapeutics Collaboration Agreement.

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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 will recognize the first $10.0 million of losses of Regulus Therapeutics as equity in loss of joint venture in its consolidated statement 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 losses of Regulus Therapeutics.

The Company accounted for its interest in Regulus Therapeutics using the equity method of accounting. Under this method, the reimbursement of expenses to the Company is recorded as a reduction to research and development expenses. At September 30, 2007, the Company s investment in the joint venture was $9.9 million, which is recorded as an investment in joint venture (Regulus Therapeutics LLC) in the consolidated balance sheets under the equity method.

7. SUBSEQUENT EVENTS

On October 31, 2007, the Company subleased from Archemix Corp. (Archemix) 22,456 rentable square feet located on a portion of the second floor of 300 Third Street in Cambridge, Massachusetts (the Sublease), which is the same location as the Company s corporate headquarters. The initial term of the Sublease will expire on September 30, 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. 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.

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ITEM 2. MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

This Quarterly Report on Form 10-Q contains forward-looking statements that involve risks and uncertainties. The statements contained in this Quarterly Report on Form 10-Q that are not purely historical are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Without limiting the foregoing, the words may, will, should, could, expects, plans, intends, anticipates, believes, estimates, predicts, potential, continue, target and similar expressions are intended to identify forward-looking statements. All forward-looking statements included in this Quarterly Report on Form 10-Q are based on information available to us up to, and including the date of this document, and we assume no obligation to update any such forward-looking statements. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain important factors, including those set forth below under this Item 2 Management s Discussion and Analysis of Financial Condition and Results of Operations, Part II, Item 1A Risk Factors and elsewhere in this Quarterly Report on Form 10-Q. You should carefully review those factors and also carefully review the risks outlined in other documents that we file from time to time with the Securities and Exchange Commission, or SEC.

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 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 new major 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 expect to apply in a systematic way to develop RNAi therapeutics for a variety of diseases.

We are building a pipeline of RNAi therapeutics. Our lead program is in Phase II clinical trials for the treatment of human respiratory syncytial virus, or RSV, infection, which we believe is the leading cause of hospitalization in infants in the United States and also occurs in the elderly and in immune compromised adults. We submitted an investigational new drug, or IND, application for ALN-RSV01 to the United States Food and Drug Administration, or FDA, in November 2005. We initiated Phase I clinical trials on this experimental drug in December 2005 in both the United States and Europe and presented results from these trials in April 2006. ALN-RSV01 was found to be safe and well tolerated when administered intranasally in these two Phase I clinical studies. In October 2006, we initiated a Phase I study with an inhaled formulation of ALN-RSV01. In November 2006, we initiated a human experimental infection study with an RSV strain designed to establish a safe and reliable RSV infection of the upper respiratory tract in adult volunteers. In May 2007, we presented results from this study that demonstrated the establishment of a safe and reliable RSV infection in the upper respiratory tract of adult volunteers. In June 2007, we initiated a Phase II experimental infection trial designed to evaluate the safety, tolerability, and anti-viral activity of ALN-RSV01 in adult subjects experimentally infected with RSV.

In pre-clinical development programs, which are programs for which we have established targeted timing for human clinical trials, we are working on a number of programs including ALN-PCS01, an RNAi therapeutic targeting a gene called PCSK9 for the treatment of hypercholesterolemia, ALN-VSP01, an RNAi therapeutic that is designed to target vascular endothelial growth factor, or VEGF, kinesin spindle protein, or KSP, for the treatment of liver cancers and potentially other cancers, and an RNAi therapeutic that is designed to target another viral respiratory infection, influenza.

We have pre-clinical discovery programs, which are programs for which we have yet to establish targeted timing for human clinical trials, focused on central nervous system, or CNS, diseases including Parkinson s disease, Huntington s disease, neuropathic pain and spinal cord injury, and progressive multifocal leukoencephalopathy, or PML, a CNS disease caused by viral infection in immune compromised patients. We also have a program focused on the inherited respiratory disease known as cystic fibrosis, or CF, as well as programs for viral hemorrhagic fever, including the Ebola virus. In connection with some of these programs as well as others still in early discovery, we

have formed alliances with leading companies, including Novartis Pharma AG, or Novartis, Biogen Idec, Inc., or Biogen Idec, and Medtronic, Inc., or Medtronic.

In August 2007, we entered into an alliance with F. Hoffmann-La Roche Ltd, or Roche, from which we received upfront payments totaling $331.0 million, which include an upfront payment under the license and collaboration agreement of $273.5 million,

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$42.5 million for the purchase of 1,975,000 of our shares issued at $21.50 per share under the common stock purchase agreement and $15.0 million for the Roche Kulmbach shares under the Alnylam Europe purchase agreement.

In September 2007, we entered into a joint venture with Isis Pharmaceuticals, Inc., or Isis, to create a new limited liability company, Regulus Therapeutics LLC, or Regulus Therapeutics, to focus on the discovery, development and commercialization of microRNA, or miRNA, therapeutics. Because miRNAs regulate whole networks of genes that can be involved in discrete disease processes, miRNA therapeutics represent a possible new approach to treat the pathways of human disease. We and Isis own 49% and 51% of Regulus Therapeutics, respectively.

We commenced operations in June 2002 and, since then, have focused our efforts primarily on business planning and development, 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 September 30, 2007, we had an accumulated deficit of $227.7 million. Through September 30, 2007, we have funded our operations primarily through the net proceeds from the sale of equity securities and payments under strategic alliances. Through September 30, 2007, a substantial portion of our total net revenues have been collaboration revenues derived from our strategic alliances with Novartis, Merck & Co., Inc., or Merck, and Roche, 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, other government and foundation funding and license fee revenues.

In September 2007, we terminated our Merck collaboration. Pursuant to the termination agreement between us and Merck, all license grants of intellectual property to develop, manufacture and/or commercialize RNAi therapeutic products under the collaboration agreement ceased as of the date of termination, 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. Accordingly, we will not receive any additional revenues from Merck in future periods.

We currently have programs focused in a number of therapeutic areas. However, we are unable to predict when, if ever, we will be able to commence sales of any product. We have never achieved profitability on a quarterly or annual basis and we expect to incur additional losses over the next several years. 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 include proceeds from the sale of equity, license and other fees, funded research and development payments, proceeds from equipment lines of credit and milestone payments under existing and future collaborative arrangements.

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. We have initiated programs to identify specific RNAi therapeutics that will be administered directly to diseased parts of the body, which we refer to as direct RNAi therapeutics, and we expect to initiate additional programs as the capabilities of our product platform evolve. All of our programs are in the early stages of development. Our most advanced development program is focused on the treatment of RSV infection. In June 2007, we initiated a Phase II experimental infection trial designed to evaluate the safety, tolerability, and anti-viral activity of ALN-RSV01 in adult subjects experimentally infected with RSV. Our other development programs are focused on the treatment of hypercholesterolemia and liver cancers. We also have discovery programs to develop direct RNAi therapeutics for the treatment of the genetic respiratory disease CF; CNS disorders, such as spinal cord injury, Parkinson s disease, Huntington s disease and neuropathic pain; hemorrhagic fever viruses, such as Ebola; PML; and several other diseases that are the subject of collaborations with Medtronic, Novartis and Biogen Idec, among others.

Drug development and approval in the United States is a multi-step process regulated by the FDA. The process begins with the filing of an IND application, which, if successful, allows the opportunity for study in humans, or clinical study, of the new drug. Clinical development typically involves three phases of study, each of which may include several different clinical trials: Phase I, II and III. The most significant costs in clinical development are in Phase III clinical trials, as they tend to be the longest and largest studies in the drug development process. Following successful completion of Phase III clinical trials, a new drug application, or NDA, must be submitted to, and accepted

by, the FDA, and the FDA must approve the NDA prior to commercialization of the drug.

There is a risk that any drug discovery and 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 drug. Moreover, there are uncertainties

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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 in which material net cash inflows are expected to commence from, any potential product candidate. These risks include the uncertainty of:

our ability to progress any product candidates into pre-clinical and clinical trials;

the scope, rate and progress of our pre-clinical trials and other research and development activities;

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 sales, marketing and distribution capabilities;

the cost of establishing 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 below under the heading Risk Factors .

Strategic Alliances

A significant component of our business strategy 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, technical resources and intellectual property to further our development efforts and to generate revenues. We have entered into license agreements with Max Planck Innovation GmbH, or Max Planck Innovation, Tekmira Pharmaceuticals Corporation, or Tekmira, Massachusetts Institute of Technology, or MIT, and Isis, as well as a number of other entities, to obtain rights to important intellectual property in the field of RNAi. We have entered into license agreements and collaborations with (1) Novartis to discover and develop therapeutics based on RNAi and to develop an RNAi therapeutic for pandemic flu, (2) Roche to develop and commercialize therapeutics based on RNAi in the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases, (3) Medtronic to develop novel drug-device products incorporating RNAi therapeutics to treat Huntington s disease and other diseases caused by degeneration of the nervous system, and (4) Biogen Idec to perform investigative research into the potential of using RNAi technology to discover and develop therapeutics to treat PML. We have also entered into contracts with government agencies, such as the National Institute of Allergy and Infectious Diseases, or NIAID, a component of the National Institutes of Health, or NIH, and the United States Department of Defense, or DoD. In addition, we have entered into an agreement with the Cystic Fibrosis Foundation Therapeutics, Inc., or CFFT, to obtain funding and technical resources for our CF program.

Joint Venture (Regulus Therapeutics LLC)

In September 2007, we entered into a joint venture with Isis to create Regulus Therapeutics to focus on the discovery, development and commercialization of miRNA therapeutics, a potential new class of drugs to treat the pathways of human disease. We and Isis own 49% and 51%, respectively, of Regulus Therapeutics. Under the terms

of the limited liability agreement, Regulus Therapeutics will be operated as an independent company and governed by a managing board comprised of an equal number of directors appointed by each of us and Isis. In consideration for our and Isis initial interests in Regulus Therapeutics, we and Isis each agreed to grant Regulus Therapeutics exclusive licenses to our intellectual property for certain miRNA therapeutic applications as well as certain patents in the miRNA therapeutics field. In addition, we agreed to make an initial cash contribution to Regulus Therapeutics of $10.0 million, resulting in us and Isis making initial capital contributions to Regulus Therapeutics of approximately equal aggregate value.

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

After a sufficient portfolio of data is obtained with respect to each miRNA compound drug candidate developed by Regulus Therapeutics, Regulus Therapeutics may elect to continue to pursue the development and commercialization of products directed to such miRNA compound and related miRNA compounds, in which event Regulus Therapeutics would be obligated to pay us and Isis a royalty on net sales of any such resulting products. If Regulus Therapeutics decides not to continue to pursue the development and commercialization of products directed to particular miRNA compounds, either we or Isis may pursue development and commercialization of such Regulus Therapeutics products. Development and commercialization of such products by either party would be subject to the payment to Regulus Therapeutics of a specified upfront fee, royalties on net sales, milestone payments upon achievement of specified regulatory events, and a portion of income received from sublicensing rights.

In connection with the execution of the limited liability agreement and the license and collaboration agreement, we also executed a services agreement with Isis and Regulus Therapeutics. Under the terms of the services agreement, we and Isis agreed to provide to Regulus Therapeutics, for the benefit of Regulus Therapeutics, certain research and development and general and administrative services, as set forth in an operating plan mutually agreed upon by us and Isis. Pursuant to this agreement, we and Isis generally will be paid by Regulus Therapeutics for these services.

We have concluded that Regulus Therapeutics qualifies as a variable interest entity under Financial Accounting Standards Board, or FASB, Interpretation No. 46R, Consolidation of Variable Interest Entities an interpretation of Accounting Research Bulletin No. 51, or FIN 46R. The limited liability agreement contains transfer restrictions on each of Isis and our limited liability company interests and, as a result, we and Isis are considered related parties under paragraph 16(d)(1) of FIN 46R. We have assessed which entity would be considered the primary beneficiary under FIN 46R and have concluded that Isis is the primary beneficiary and, accordingly, we have not consolidated Regulus Therapeutics. We account for our investment in Regulus Therapeutics using the equity method of accounting. Under this method, the reimbursement of expenses to us is recorded as a reduction to research and development expenses. We will recognize the first $10.0 million of losses of Regulus Therapeutics as equity in loss of joint venture in our consolidated statement of operations because we are responsible for funding those losses through our initial $10.0 million cash contribution. Thereafter, we will recognize 49% of the losses of Regulus Therapeutics. At September 30, 2007, our investment in the joint venture was $9.9 million, which is recorded as an investment in joint venture (Regulus Therapeutics LLC) in the consolidated balance sheets under the equity method.

Critical Accounting Policies and Estimates

There have been two significant changes to our critical accounting policies since the beginning of this fiscal year related to revenue recognition and accounting for income taxes. Our other critical accounting policies are described in the Management Discussion and Analysis of Financial Condition and Results of Operations section of our Annual Report on Form 10-K for the year ended December 31, 2006, which we filed with the SEC on March 12, 2007.

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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 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 Issue No. 00-21, Accounting for Revenue Arrangements with Multiple Deliverables, or EITF 00-21, Emerging Issues Task Force Issue No. 99-19, Reporting Revenue Gross as a Principal Versus Net as an Agent, and Emerging Issues Task Force Issue No. 01-9, Accounting for Consideration Given by a Vendor to a Customer (Including a Reseller of the Vendor s Products), or EITF 01-9.

Non-refundable license fees are recognized as revenue when 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 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 would then be accounted for separately as performed. If the license is considered to either not have stand-alone value or have standalone 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 provided 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. 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

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cumulative amount of payments received or the cumulative amount of revenue earned, as determined using the proportional performance method, as of each reporting period.

If we cannot reasonably estimate the level of effort required to complete our performance obligations under an arrangement, then revenue under the arrangement would 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 basis, 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.

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 of 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 September 30, 2007, we have short-term and long-term deferred revenue of $61.7 million and $217.0 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.

The estimate of deferred revenue also reflects management s estimate of the periods of our involvement in certain of our collaborations. Our performance

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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.

Roche

We have initially recorded $278.5 million as deferred revenue in connection with the Roche alliance. This amount represents the aggregate proceeds received from Roche, $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 $1.2 million. Roche is also required to make payments to us upon achievement of specified development and sales milestones set forth in the license and collaboration agreement and royalty payments based on worldwide annual net sales, if any, of RNAi therapeutic products by Roche, its affiliates and sublicensees. In addition, we have also 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 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 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 initially recording 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 reasonable estimates of our remaining efforts under the collaboration, we will modify the method of recognition and utilize proportional performance method. As future milestones are achieved, and to the extent they are within the five year term, the amounts will be recognized as revenue prospectively over the remaining period of performance.

Accounting for Income Taxes

Effective January 1, 2007, we adopted the provisions of FASB Interpretation No. 48 Accounting for Uncertainty in Income Taxes-an interpretation of FASB Statement 109, or FIN 48, which clarifies

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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 statement 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.

At December 31, 2006, we had federal and state net operating loss, or NOL, carryforwards of $54.4 million and $53.6 million, respectively, available to reduce future taxable income and which will expire at various dates beginning in 2008 through 2026. At December 31, 2006, federal and state research and development and other credit carryforwards were $1.8 million and $1.0 million, respectively, available to reduce future tax liabilities, and that will expire at various dates beginning in 2018 through 2026. We have concluded that it is more likely than not that our deferred tax assets, including those associated with these carryforwards, will not be realized and, accordingly, have recorded a full valuation allowance. This assessment was based on our estimates of future taxable income which involve significant judgment.

Results of Operations

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2007	**2006**	**2007**	**2006**
Net revenues from research collaborators	$ 16,315	$ 8,211	$ 32,665	$ 19,949
Operating expenses	67,653	16,815	122,950	49,459
Loss from operations	(51,338)	(8,604)	(90,285)	(29,510)
Net loss	$ (52,792)	$ (7,400)	$ (87,128)	$ (26,170)

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Revenues

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2007	2006	2007	2006
Roche	$ 6,385	$	$ 6,385	$
Novartis	2,891	6,445	11,416	17,229
Other research collaborators	6,669	238	13,721	754
InterfeRx program, research reagent licenses and other	370	1,528	1,143	1,966
Total net revenues from research collaborators	$ 16,315	$ 8,211	$ 32,665	$ 19,949

Revenues increased significantly for the three and nine months ended September 30, 2007 as compared to the three and nine months ended September 30, 2006 primarily as a result of our August 2007 alliance with Roche and the termination of our collaboration with Merck. We received upfront payments totaling $331.0 million under the Roche alliance, of which $53.1 million was allocated to the purchase of 1,975,000 of our shares issued under the common stock purchase agreement and $278.5 million is being recognized as revenue on a straight-line basis over five years under the Roche alliance. The Alnylam Europe Purchase Agreement also includes transition services to be performed by Roche Kulmbach employees at various levels through August 2008. We will reimburse Roche for these services at an agreed-upon rate. We are recording these services as contra revenue (a reduction of revenues) in the period incurred.

In September 2007, we terminated our Merck collaboration agreement. 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 represents all of the remaining deferred revenue under the Merck agreement.

The decrease in Novartis revenues in the three months ended September 30, 2007 compared to the three months ended September 30, 2006 was due to quarterly fluctuations in the number of resources allocated to the Novartis main alliance. The decrease in Novartis revenues was also due to a decrease in the number of resources allocated to the Novartis flu program as a result of the program being taken off the development path during 2007. The decrease in Novartis revenues in the nine months ended September 30, 2007 compared to the nine months ended September 30, 2006 was due to a decrease in the number of resources allocated to our Novartis alliances as well as lower external expense reimbursement under our Novartis flu alliance as a result of the program being taken off the development path during 2007.

In the three and nine months ended September 30, 2007, other research collaborators revenues consisted of expense reimbursement and amortization revenues from Biogen Idec, Merck and NIH for Ebola. The increase in other research collaborators revenues in both periods is primarily the result of new collaborations with Biogen Idec and the NIH, which both began in the fourth quarter of 2006.

The decrease in InterfeRx program, research reagent licenses and other revenues for the three and nine months ended September 30, 2007 compared to the three and nine months ended September 30, 2006 was due to upfront payments pursuant to license agreements entered into under our InterfeRx program in the prior year.

Total deferred revenue of $278.7 million at September 30, 2007 consists of payments received from collaborators, primarily Roche, pursuant to license agreements that we have yet to earn pursuant to our revenue recognition policies.

For the foreseeable future, we expect our revenues to continue to be derived primarily from strategic alliances, collaborations and licensing activities and to continue to increase significantly as a result of our August 2007 alliance with Roche.

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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:

	Three Months Ended September 30, 2007	% of Total Operating Expenses	Three Months Ended September 30, 2006	% of Total Operating Expenses	Increase $	Increase %
Research and development	$ 59,618	88%	$ 12,697	76%	$ 46,921	370%
General and administrative	8,035	12%	4,118	24%	3,917	95%
Total operating expenses	$ 67,653	100%	$ 16,815	100%	$ 50,838	302%

	Nine Months Ended September 30, 2007	% of Total Operating Expenses	Nine Months Ended September 30, 2006	% of Total Operating Expenses	Increase $	Increase %
Research and development	$ 105,102	85%	$ 37,003	75%	$ 68,099	184%
General and administrative	17,848	15%	12,456	25%	5,392	43%
Total operating expenses	$ 122,950	100%	$ 49,459	100%	$ 73,491	149%

Research and development

The following tables summarize 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:

	Three Months Ended September 30, 2007	% of Expense Category	Three Months Ended September 30, 2006	% of Expense Category	Increase $	Increase %
Research and development						
License fees	$ 33,520	56%	$ 2,829	22%	$ 30,691	1085%
Clinical trial and manufacturing	6,729	11%	1,179	9%	5,550	471%

External services	6,374	11%	1,626	13%	4,748	292%
Non-cash stock-based compensation	5,667	10%	883	7%	4,784	542%
Compensation-related	3,475	6%	2,863	22%	612	21%
Facilities-related	1,831	3%	1,623	13%	208	13%
Lab supplies and materials	1,482	2%	1,228	9%	254	21%
Other	540	1%	466	5%	74	16%
Total research and development	$ 59,618	100%	$ 12,697	100%	$ 46,921	370%

As indicated in the table above, the increase in research and development expenses in the three months ended September 30, 2007 as compared to the three months ended September 30, 2006 was due primarily to an increase in license fees consisting of $27.5 million in payments due to certain entities, primarily Isis, as a result of the Roche alliance and $6.0 million in payments for delivery related activities. The increase was also due to an increase in clinical trial expenses in support of our clinical program for RSV, which began Phase II trials in June 2007. The increase in external services was due to higher expenses related to our pre-clinical programs

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for the treatment of hypercholesterolemia, liver cancer and Ebola, as well as higher expenses associated with our delivery related collaborations. 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 and higher non-employee stock compensation charges.

We expect to continue to devote a substantial portion of our resources to research and development expenses and, excluding the impact of the license fees we paid as a result of the Roche alliance, we expect that research and development expenses will increase as we continue development of our and our collaborators product candidates and focus on delivery related technologies.

	Nine Months Ended September 30, 2007	% of Expense Category	Nine Months Ended September 30, 2006	% of Expense Category	Increase $	Increase %
Research and development						
License fees	$ 42,156	40%	$ 3,954	11%	$ 38,202	966%
Clinical trial and manufacturing	18,153	17%	7,618	21%	10,535	138%
External services	14,453	14%	4,451	12%	10,002	225%
Compensation-related	10,087	10%	7,743	21%	2,344	30%
Non-cash stock-based compensation	7,687	7%	3,331	9%	4,356	131%
Facilities-related	6,035	6%	4,506	12%	1,529	34%
Lab supplies and materials	4,885	5%	4,174	11%	711	17%
Other	1,646	1%	1,226	3%	420	34%
Total research and development	$ 105,102	100%	$ 37,003	100%	$ 68,099	184%

As indicated in the table above, the increase in research and development expenses in the nine months ended September 30, 2007 as compared to the nine months ended September 30, 2006 was due primarily to an increase in license fees, including $27.5 million in payments due to certain entities, primarily Isis, as a result of the Roche alliance and $14.3 million in charges for licenses for certain delivery technologies. The increase was also due to an increase in clinical trial expenses in support of our clinical program for RSV, which began Phase II trials in June 2007. Also contributing to the increase were higher manufacturing and external service costs associated with our pre-clinical programs for the treatment of hypercholesterolemia, liver cancer and Ebola, as well as costs related to an increase in research and development headcount over the past year to support our expanding pipeline and alliances. 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 and higher non-employee stock compensation charges.

We do not track most of our research and development costs 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. 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. 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.

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General and administrative

The following tables summarize 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:

	Three Months Ended September 30, 2007	% of Expense Category	Three Months Ended September 30, 2006	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
General and administrative						
Consulting and professional services	$ 2,887	36%	$ 1,073	26%	$ 1,814	169%
Non-cash stock-based compensation	2,255	28%	831	20%	1,424	171%
Compensation-related	1,279	16%	921	22%	358	39%
Facilities-related	845	11%	751	18%	94	13%
Insurance	168	2%	171	4%	(3)	(2%)
Other	601	7%	371	10%	230	62%
Total general and administrative	$ 8,035	100%	$ 4,118	100%	$ 3,917	95%

As indicated in the table above, the increase in general and administrative expenses during the three months ended September 30, 2007 as compared to the three months ended September 30, 2006 was due primarily to higher professional service fees, which were the result of increased business development activities, including work related to our alliance with Roche, our joint venture with Isis, Regulus Therapeutics, and the amendment and restatement of our Medtronic agreement, as well as higher costs supporting overall corporate growth. 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 and higher non-employee stock compensation charges.

	Nine Months Ended September 30, 2007	% of Expense Category	Nine Months Ended September 30, 2006	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
General and administrative						
Consulting and professional services	$ 6,428	36%	$ 3,733	30%	$ 2,695	72%
Non-cash stock-based compensation	4,181	23%	2,364	19%	1,817	77%
Compensation-related	3,367	19%	2,609	21%	758	29%
Facilities-related	1,870	10%	2,009	16%	(139)	(7%)
Insurance	496	3%	488	4%	8	2%
Other	1,506	9%	1,253	10%	253	20%

Total general and administrative	$ 17,848	100%	$ 12,456	100%	$ 5,392	43%

As indicated in the table above, the increase in general and administrative expenses during the nine months ended September 30, 2007 as compared to the nine months ended September 30, 2006 was due primarily to higher professional service fees, which were the result of increased business development activities, including work related to our alliance with Roche, our joint venture with Isis, Regulus Therapeutics, as well as higher costs supporting overall corporate growth. 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 and higher non-employee stock compensation charges.

Interest income, interest expense and other

Interest income was $4.3 million and $9.6 million for the three and nine months ended September 30, 2007, respectively, compared to $1.6 million and $4.4 million for the three and nine months ended September 30, 2006, respectively. The increase in both periods was due to our higher average cash, cash equivalent and marketable securities balances primarily as a result of $101.1 million in proceeds we received from our December 2006 public offering of common stock as well as the $331.0 million in proceeds we received in August 2007 from our alliance with Roche.

Interest expense was $0.3 million and $0.8 million for the three and nine months ended September 30, 2007, respectively, compared to $0.3 million and $0.7 million for the three and nine months ended September 30, 2006, respectively. Interest expense in each year related to borrowings under our lines of credit used to finance capital equipment purchases.

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Liquidity and Capital Resources

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

	Nine Months Ended September 30,	
	2007	**2006**
Net loss	$ (87,128)	$ (26,170)
Adjustments to reconcile net loss to net cash used in operating activities	25,189	8,784
Changes in operating assets and liabilities	266,896	(2,631)
Net cash provided by (used in) operating activities	204,957	(20,017)
Net cash used in investing activities	(189,737)	(25,207)
Net cash provided by financing activities	57,880	64,935
Effect of exchange rate on cash	(508)	48
Net increase in cash and cash equivalents	72,592	19,759
Cash and cash equivalents, beginning of period	127,955	15,757
Cash and cash equivalents, end of period	$ 200,547	$ 35,516

Since we commenced operations in 2002, we have generated significant losses. At September 30, 2007, we had an accumulated deficit of $227.7 million. At September 30, 2007, we had cash, cash equivalents and marketable securities of $468.4 million, compared to cash, cash equivalents and marketable securities of $217.3 million at December 31, 2006. The increase in our cash, cash equivalents and marketable securities at September 30, 2007 was due to our receipt of $331.0 million of up-front cash payments received under our Roche alliance. 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.

Operating activities

We have required significant amounts of cash to fund our operating activities as a result of net losses since our inception. The increase in net cash provided by operating activities for the nine months ended September 30, 2007 compared to the nine months ended September 30, 2006 was due primarily to the proceeds received from our August 2007 Roche alliance. Offsetting the proceeds from the Roche alliance, the main components of our use of cash in operating activities for the nine months ended September 30, 2007 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 used in operating activities. These non-cash adjustments primarily consist of non-cash license fees, stock-based compensation, depreciation and amortization. We had an increase in deferred revenue of $260.1 million for the nine months ended September 30, 2007, due to the proceeds received from our Roche alliance. Additionally, accrued expenses and collaboration receivables increased $7.1 million and $1.2 million, respectively, for the nine months ended September 30, 2007. 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 nine months ended September 30, 2007, net cash used in investing activities of $189.7 million resulted primarily from net purchases of marketable securities of $178.5 million. Also included in our investing activities for the nine months ended September 30, 2007 was a $10.0 million cash contribution in connection with the creation of

Regulus Therapeutics. For the nine months ended September 30, 2006, net cash used in investing activities resulted from net purchases of marketable securities of $20.5 million, as well as purchases of property and equipment of $4.7 million.

Financing activities

For the nine months ended September 30, 2007, net cash provided by financing activities was $57.9 million compared to $64.9 million for the nine months ended September 30, 2006. The main components of net cash provided by financing activities for the nine months ended September 30, 2007 consisted primarily of the proceeds of $42.5 million from our sale of 1,975,000 shares of common stock to Roche in connection with the establishment of the Roche alliance. For the nine months ended September 30, 2006, net cash provided by financing activities was primarily a result of the net proceeds of $62.2 million from our follow-on public offering in January 2006.

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In March 2006, we entered into an agreement with Oxford Finance Corporation, or 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. Of such amount, $1.3 million bears interest at fixed rates ranging from 10.1% to 10.4% and is being repaid in 48 monthly installments of principal and interest. The remainder of such amount, $2.9 million, bears interest at fixed rates ranging from 10.0% to 10.4% and is being repaid in 36 monthly installments of principal and interest. In May 2007, we borrowed an aggregate of $1.0 million from Oxford pursuant to the agreement. Of such amount, $0.6 million bears interest at a fixed rate of 10% and is being repaid in 48 monthly installments of principal and interest. The remainder of such amount, $0.4 million, bears interest at a fixed rate of 10% and is being repaid in 36 monthly installments of principal and interest.

In March 2004, we entered into an equipment line of credit with Lighthouse Capital Partners to finance leasehold improvements and equipment purchases of up to $10.0 million. The outstanding principal bears interest at a fixed rate of 9.25%, except for the drawdown made in December 2005 which bears interest at a fixed rate of 10.25%. The outstanding principal matures at various dates through December 2009. We were required to make interest-only payments on all draw-downs made during the period from March 26, 2004 through September 30, 2005, at which point all draw-downs began to be repaid over 48 months. On the maturity of each equipment advance under the line of credit, we are required to pay, in addition to the principal and interest due, an additional amount of 11.5% of the original principal. This amount is being accrued over the applicable borrowing period as additional interest expense.

As of September 30, 2007, we had an aggregate outstanding balance of $7.7 million under our loan agreements.

Based on our current operating plan, we believe that our existing resources, together with the cash we expect to generate under our current alliances, including our Roche alliance, 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 products, extend the capabilities of our technology platform, conduct clinical trials 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.

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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 the following:

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 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.

Contractual Obligations and Commitments

The disclosure of our contractual obligations and commitments is set forth under the heading Management s Discussion and Analysis of Financial Condition and Results of Operations Contractual Obligations and Commitments in our Annual Report on Form 10-K for the year ended December 31, 2006. Since December 31, 2006, we agreed to make available to Tekmira a $5.0 million loan for capital equipment expenditures related to manufacturing services performed by Tekmira beginning in 2008. There have been no other material changes in our contractual obligations and commitments since December 31, 2006.

Recently Issued Accounting Pronouncements

In September 2006, the FASB issued Statement of Financial Standards, or SFAS, No. 157, Fair Value Measurements, or SFAS No. 157. SFAS No. 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. SFAS No. 157 is expected to be effective for financial statements issued for fiscal years beginning after November 15, 2007, and interim periods within those fiscal years, with early adoption permitted. We are evaluating the implications of this standard, but currently we do not expect it to have a significant impact on our consolidated financial statements.

In February 2007, the FASB issued SFAS No. 159, The Fair Value Option for Financial Assets and Financial Liabilities-including an amendment of FAS 115, or SFAS No. 159. The new statement allows entities to choose, at specified election dates, to measure eligible financial assets and liabilities at fair value that are not otherwise required to be measured at fair value. If a company elects the fair value option for an eligible item, changes in that item s fair value in subsequent reporting periods must be recognized in current earnings. SFAS No. 159 is effective for fiscal years beginning after November 15, 2007. We are evaluating the potential impact of SFAS No. 159 on our consolidated financial statements.

In September 2007, the FASB reached a consensus on Emerging Issues Task Force Issue No. 07-03, Accounting for Nonrefundable Advance Payments for Goods or Services to Be Used in Future Research and Development

Activities, or EITF 07-03. EITF 07-03 requires companies to defer and capitalize, until the goods have been delivered or the related services have been rendered, non-refundable advance payments for goods that will be used or services that will be performed in future research and development activities. EITF 07-03 is effective for fiscal years beginning after December 15, 2007. We do not expect EITF 07-03 will have a material impact on our consolidated financial statements.

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ITEM 3. 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, corporate debt 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 are sensitive to changes in interest rates. 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 September 30, 2007 would impact the net fair value of such interest-sensitive financial instruments by approximately $1.4 million.

ITEM 4. 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 September 30, 2007. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, or 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 September 30, 2007, our 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.

No change in our internal control over financial reporting (as defined in Rules 13a 15(d) and 15d 15(d) under the Exchange Act) occurred during the quarter ended September 30, 2007 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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PART II. OTHER INFORMATION

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 Quarterly Report on Form 10-Q 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 undertake no obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise. 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 an unproven technology;

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 relationships; 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 drugs 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 RNAi technology. Neither we nor any other company has received regulatory approval to market therapeutics utilizing small interfering RNAs, or 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.

In addition, there are also substantial challenges to achieving effective RNAi therapeutics based on the need to achieve efficient delivery into cells and tissues in a clinically relevant manner and at doses that are cost-effective. We are working internally and with external collaborators to develop the ability to deliver our RNAi therapeutics directly to specific cell types, including our RSV product. In addition, we are working to extend our capabilities to enable the development of RNAi therapeutics that travel through the bloodstream to reach diseased parts of the body, which we refer to as Systemic RNAi[tm] and are developing technology to achieve efficient and safe systemic delivery. If we are

unable to achieve either local or systemic delivery of our RNAi therapeutics to the relevant cell types, our RNAi therapeutics will not be effective.

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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 September 30, 2007, we had an accumulated deficit of $227.7 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 collaborations with pharmaceutical companies or funding from contracts with the government, but cannot be certain that we will be able to secure or maintain these collaborations or contracts or to 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 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;

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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 establish and maintain 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; 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. While the exercise of these rights may provide us with additional funding under some circumstances, the 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 financial statements prove inaccurate, our actual results may vary from those reflected in our projections and accruals.

Our financial statements have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these 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.

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 will select disease targets towards which the parties will collaborate to develop drug candidates. Novartis will pay a portion of the costs to develop these drug candidates and will commercialize and market any products derived from this collaboration. In addition, Novartis will pay us certain pre-determined amounts based on the achievement of pre-clinical and clinical milestones as well as royalties on the annual net sales of any products derived from this collaboration. This collaboration has an initial term of three years that may be extended by Novartis for two additional one-year terms. Novartis may elect to terminate this collaboration in the event of a material uncured breach by us. We expect that a substantial amount of the funding for our operations 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 our intellectual property into Novartis operations and develop products without our involvement for a pre-determined fee. 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

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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 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 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 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 with other parties.

Our license and collaboration agreement with Roche is important to our business. If Roche does not successfully develop drugs pursuant to this license and collaboration agreement or this license and collaboration agreement results in competition between us and Roche for the development of drugs targeting the same diseases, our business could be adversely affected.

In July 2007, we and, for limited purposes, Alnylam Europe, entered into a license and collaboration agreement with Roche. The license and collaboration agreement provides for the grant to Roche of 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 as well as our collaboration agreements. The license is initially limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases, which may be expanded to include other therapeutic areas under certain circumstances. As such, Roche could become a competitor of ours in the development of RNAi-based drugs targeting the same diseases. Roche 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 Roche in the development of RNAi-based drugs targeting the same disease. Roche is required to make payments to us upon achievement of specified development and sales milestones set forth in the license and collaboration agreement and royalty payments based on worldwide annual net sales, if any, of RNAi therapeutic products by Roche, its affiliates and sublicensees. If Roche fails to successfully develop products using this technology, we may not receive any such milestone or royalty payments.

We may not be able to execute our business strategy if we are unable to enter into alliances with other companies that can provide 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. Accordingly, we have entered into alliances with other companies that can provide such capabilities and may need to enter into additional alliances in the future. For example, we may enter into alliances with major pharmaceutical companies to jointly develop specific drug candidates and to jointly commercialize them if they are approved. In such alliances, we would expect our pharmaceutical collaborators to provide substantial capabilities in clinical development, regulatory affairs, marketing and sales. We may not be successful in entering into any 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 Medtronic, Biogen Idec, Department of Defense and the 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 this 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.

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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. 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. In addition, 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 of its own development.

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.

The Board of Directors of Biogen Idec authorized management to evaluate whether third parties would have an interest in acquiring Biogen Idec. It is possible that the decision to explore a potential acquisition, and/or the subsequent consummation of any acquisition could have an impact on our collaboration with Biogen Idec. We intend to monitor our collaboration in the light of the facts and circumstances surrounding a potential change in control of Biogen Idec.

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 may be negatively affected.

In September 2006, the 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, the government has committed to pay us $14.2 million over the first two years of the contract and, subject to budgetary considerations in future years, the remaining $8.8 million over the last 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.

In August 2007, we were awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus infection with the Department of Defense. This federal contract is expected to provide us with up to $38.6 million in funding through the second quarter of 2010 to develop RNAi therapeutics for hemorrhagic fever virus infection. This contract is with the Defense Threat Reduction Agency 2007 Medical Science and Technology Chemical and Biological Defense Transformational Medical Technologies Initiative, the mission of which is to provide state-of-the-art defense capabilities to U.S. military personnel by addressing traditional and non-traditional biological threats. Of the $38.6 million in funding, the government has committed to pay us up to $7.2 million through April 2008 and, subject to the progress of the program and budgetary considerations in future years, the remaining $31.4 million over the last two years of the contract. If we do not receive the $38.6 million we expect to receive under this contract, we may not be able to develop therapeutics to treat hemorrhagic fever virus

infection.

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

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We and Isis created Regulus Therapeutics to discover, develop and commercialize microRNA therapeutics. Formed as a joint venture, 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 antagonists independently of Regulus. If Regulus Therapeutics is unable to discover, develop and commercialize microRNA 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. The limited liability company agreement provides that following such initiation of 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 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 miRNA 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 at all or in a timely manner. 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 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. In addition, to fulfill our siRNA requirements we may need to secure alternative suppliers of synthetic siRNAs. The manufacturing process for any products that we may develop is subject to the FDA or foreign regulatory authority approval process and we will need to contract with manufacturers who can meet all applicable FDA or 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 production. 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 applications for regulatory approvals for our products;
- 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.

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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 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 expect to depend significantly on third parties who may not successfully commercialize our products.

We have no sales, marketing or distribution experience. We expect to rely heavily on third parties to launch and market certain of our product candidates, if approved. 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.

To develop internal sales, distribution and marketing capabilities, we will have to invest significant amounts of 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.

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 President and 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 key employees.

Although we have generally been successful in our recruiting efforts, we face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions. 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. Prior to our sale of our Kulmbach facility to Roche, we employed approximately 140 full time equivalent employees, with offices and laboratory space in both Cambridge, Massachusetts and Kulmbach, Germany. As of September 30, 2007, we had approximately 100 employees in our facility in Cambridge, Massachusetts. We have access to our former employees in our Kulmbach facility who currently work for Roche for a transition period, after which we will no longer have access to the employees in that facility. We intend to rebuild the capacity from our Kulmbach operation in Cambridge, Massachusetts. However, we may not be able to find, successfully recruit and retain individuals capable of reproducing the operations formerly performed in Kulmbach, Germany. Any failure to successfully rebuild the operations that were formerly performed in Kulmbach could have a material adverse effect on our business.

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In addition, 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.

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 respiratory syncytial virus, or RSV, infection. We completed two Phase I clinical trials of ALN-RSV01 in 2006 and began an additional Phase I clinical trial in October 2006. In November 2006, we announced that we had initiated a human experimental infection study with RSV. In May 2007, we presented results from this study that demonstrated the establishment of a safe and reliable RSV infection in the upper respiratory tract of adult volunteers. In June 2007, we initiated 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 may not be able to further advance this or any other product candidate through clinical trials. If we successfully enter into clinical studies, the results from pre-clinical testing of a drug candidate may not predict the results that will be obtained in subsequent human 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 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 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;

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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 candidate; 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, or PD, Huntington s disease, or 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 U.S. 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.

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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.

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 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 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; and

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.

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Even if we obtain regulatory approvals, our marketed drugs will be subject to ongoing regulatory review. If we fail to comply with continuing U.S. 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 and/or benefits of the treatments.

Even if we develop RNAi therapeutic products for the prevention or treatment of infection by pandemic flu virus and/or hemorrhagic fever viruses such as Ebola, governments may not elect to purchase such products, 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 pandemic flu or 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 flu program is to develop RNAi therapeutic targeting gene sequences that are highly conserved across known flu viruses, if the sequence of any flu 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

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pandemic flu could be stockpiled by governments as part of their preparations for a flu pandemic, they may not elect to purchase such product.

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;

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 and the 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 challenging the prices charged for medical 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 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;

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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 recently enacted in the United States 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.

Another development that may affect the pricing of drugs is Congressional action regarding drug reimportation into the United States. The Medicare Prescription Drug Plan legislation, which became law in December 2003, required the Secretary of Health and Human Services to promulgate regulations for drug reimportation from Canada into the United States under some circumstances, including when the drugs are sold at a lower price than in the United States. The Secretary, however, retained the discretion not to implement a drug reimportation plan if he finds that the benefits do not outweigh the costs, and has so far declined to approve a reimportation plan. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. Legislation or regulations allowing the reimportation of drugs, if enacted, could decrease the price we receive for any products that we may develop, negatively affecting our anticipated revenues and prospects for profitability.

Some states and localities have established drug importation programs for their citizens, and federal drug import legislation has been introduced in Congress. The FDA has warned that imported drugs may be unsafe or illegal. If such programs become more widespread or the federal government changes its position against drug importation, prices we receive for any products that we may develop may decrease, negatively affecting our anticipated revenues and prospects for profitability.

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.

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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 and until recently, in Germany 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 and the procedures we employed in our German facility comply with the standards mandated by applicable German laws and guidelines. 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 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 and marketing pharmaceutical products;
- 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, flu, hypercholesterolemia, liver cancer, PML, Ebola, HD, PD, neuropathic pain, and CF. Virazole is currently marketed for the treatment of certain RSV patients, Tamiflu® and Relenza® are marketed for the treatment of flu patients, numerous drugs are currently marketed or used for the treatment of hypercholesterolemia, liver cancer, PD and neuropathic pain and two drugs, TOBI® and Pulmozyme®, are currently marketed for the treatment of CF. 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;

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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 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 other companies that are working in the field of RNAi. In addition, we granted licenses to Isis, GeneCare, Benitec, Nastech, Calando, Tekmira, Quark as well as 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 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.

In addition, as a result of agreements that we have entered into, Roche has 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.

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 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.

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Our strategy depends on our ability to rapidly identify and seek patent protection for our discoveries. In addition, we will 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. The issuance of a patent does not guarantee that it is valid or enforceable. Any patents we have obtained, or obtain in the future, may be challenged, invalidated, unenforceable or circumvented. Moreover, 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. 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 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, the Massachusetts Institute of Technology, the Whitehead Institute for Biomedical Research, Max Planck Innovation, Stanford University, and Tekmira. 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 assert patent rights that prevent us from developing and commercializing our products.

RNA interference is a relatively new scientific field that has generated many different patent applications from organizations and individuals seeking to obtain important patents in the field. We have obtained important grants and issuances of RNAi patents and have in-licensed many patents on an exclusive basis. Our patents and patent applications claim many different methods, compositions and processes relating to the discovery, development and commercialization of RNAi therapeutics. As the field is maturing, patent applications are being fully processed by government patent offices around the world. There can be uncertainty about which patents will issue, when, to whom, and with what claims. It is likely that there will be significant litigation and other proceedings, such as interference and opposition proceedings in various patent offices, relating to patent rights in the RNAi field. Others may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes among third parties could lead to the weakening or invalidation of our intellectual property rights. Any attempt to circumvent or invalidate

our intellectual property rights would be costly, would require significant time and attention of our management and could have a material adverse effect on our business.

After the grant by the European Patent Office, or EPO, of the Kreutzer-Limmer patent, published under publication number EP 1144623B9, several oppositions to the issuance of the European patent were filed with the EPO, a practice that is allowed under the European Patent Convention, or EPC. In oral proceedings in September 2006, the EPO opposition division in charge of the opposition proceedings upheld the patent with amended claims. This decision has been appealed by two of the opponents, including

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Sirna Therapeutics, which was acquired by Merck in December 2006, and Silence Therapeutics. Based on the appeal, the Boards of Appeal of the EPO may choose to uphold, further amend or revoke the patent it in its entirety. However, because a European Patent represents a bundle of national patents for each of the designated member states and must be enforced on a country-by country-basis, even if upheld, a National Court in one or more of the EPC member states could subsequently rule the patent invalid or unenforceable. In addition, National Courts in different countries could come to differing conclusions in interpreting the scope of the upheld claims.

In addition, four parties have filed Notices of Opposition in the EPO against a second Kreutzer-Limmer patent, published under the publication number EP 1214945, and one party has given notice to the Australian Patent Office, IP Australia, that it opposes the grant of our patent AU 778474, which derives from the same parent international patent application that gave rise to EP 1144623 and EP 1214945. Furthermore, one party has filed a notice of opposition regarding the European Patent EP 1352061, the European regional phase of a patent family commonly referred to as Kreutzer-Limmer II. The proceedings in the EPO and Australian Patent Office may take several years before an outcome becomes final.

There are also 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 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 will 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.

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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 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.

Novartis held approximately 13% of our outstanding common stock as of September 30, 2007. 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.

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

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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 6. EXHIBITS

10.1	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
10.2	Common Stock Purchase Agreement dated as of July 8, 2007 between the Registrant and Roche Finance Ltd
10.3	Share Purchase Agreement, dated as of July 8, 2007, among Alnylam Europe AG, the Registrant and Roche Pharmaceuticals GmbH
10.4	Amended and Restated Collaboration Agreement, entered into as of July 27, 2007, by and between the Registrant and Medtronic, Inc.
10.5	License and Collaboration Agreement, entered into as of September 6, 2007, by and among the Registrant, Isis Pharmaceuticals, Inc. and Regulus Therapeutics LLC
10.6	Limited Liability Company Agreement of Regulus Therapeutics LLC, dated as of September 6, 2007
10.7	Termination Agreement, dated as of September 18, 2007, by and between Merck & Co., Inc. and the Registrant
31.1	Certification of principal executive officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2	Certification of principal financial officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1	Certification of principal executive officer pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code.
32.2	Certification of principal financial officer pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code.

Confidential treatment requested as to certain portions, which portions have been omitted and filed separately with the Securities and Exchange Commission.

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized.

ALNYLAM PHARMACEUTICALS, INC.

Date: November 8, 2007

By: /s/ John M. Maraganore
John M. Maraganore, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Date: November 8, 2007

By: /s/ Patricia L. Allen
Patricia L. Allen
Vice President of Finance and Treasurer
(Principal Financial and Accounting Officer)