

ALNYLAM PHARMACEUTICALS, INC.

Form 10-Q

August 09, 2007

**Table of Contents**

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

**FORM 10-Q**

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

**For the quarterly period ended June 30, 2007**

**OR**

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

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

**Commission File Number 000-50743**

**ALNYLAM PHARMACEUTICALS, INC.**

(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction of  
incorporation or organization)

77-0602661  
(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 ☒ No ☐

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 ☐ Accelerated filer ☒ Non-accelerated filer ☐

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

As of July 31, 2007, the registrant had 37,694,672 shares of Common Stock, \$0.01 par value per share, outstanding.

## INDEX

	<b>PAGE NUMBER</b>
<b>PART I. FINANCIAL INFORMATION</b>	
ITEM 1. FINANCIAL STATEMENTS (Unaudited)	
<u>CONDENSED CONSOLIDATED BALANCE SHEETS AS OF JUNE 30, 2007 AND DECEMBER 31, 2006</u>	1
<u>CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS FOR THE THREE AND SIX MONTHS ENDED JUNE 30, 2007 AND 2006</u>	2
<u>CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS FOR THE SIX MONTHS ENDED JUNE 30, 2007 AND 2006</u>	3
<u>NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS</u>	4
 <u>ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS</u>	 12
 <u>ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK</u>	 22
 <u>ITEM 4. CONTROLS AND PROCEDURES</u>	 22
<b>PART II. OTHER INFORMATION</b>	
 <u>ITEM 1A. RISK FACTORS</u>	 23
 <u>ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS</u>	 40
 <u>ITEM 6. EXHIBITS</u>	 41
<u>SIGNATURES</u>	
<u>Ex-31.1 Certification of principal executive officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended</u>	
<u>Ex-31.2 Certification of principal financial officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended</u>	
<u>Ex-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</u>	
<u>Ex-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</u>	

Table of Contents

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

	<b>June 30, 2007</b>	<b>December 31, 2006</b>
<b>ASSETS</b>		
<b>Current assets:</b>		
Cash and cash equivalents	\$ 84,464	\$ 127,955
Marketable securities	110,304	89,305
Collaboration receivables	5,615	3,829
Prepaid expenses and other current assets	1,575	1,695
Total current assets	201,958	222,784
Property and equipment, net	12,965	12,173
Intangible assets, net	1,737	1,933
Restricted cash	2,313	2,313
Other assets	685	803
Total assets	\$ 219,658	\$ 240,006
<b>LIABILITIES AND STOCKHOLDERS EQUITY</b>		
<b>Current liabilities:</b>		
Accounts payable	\$ 5,669	\$ 4,085
Accrued expenses	9,980	4,479
Current portion of notes payable	3,617	3,217
Deferred revenue	7,840	11,144
Total current liabilities	27,106	22,925
Deferred revenue, net of current portion	5,105	6,786
Deferred rent	3,271	3,202
Notes payable, net of current portion	4,906	5,919
Total liabilities	40,388	38,832
Commitments and contingencies		
<b>Stockholders equity:</b>		
Preferred stock, \$0.01 par value, 5,000,000 shares authorized and no shares issued and outstanding at June 30, 2007 and December 31, 2006		
Common stock, \$0.01 par value, 125,000,000 shares authorized; 37,635,786 and 37,050,631 shares issued and outstanding at June 30, 2007 and December 31, 2006, respectively	376	371
Additional paid-in capital	353,221	340,779
Deferred stock compensation	(22)	(89)
Accumulated other comprehensive income	558	640
Accumulated deficit	(174,863)	(140,527)

Total stockholders' equity	179,270	201,174
Total liabilities and stockholders' equity	\$ 219,658	\$ 240,006

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

1

---

Table of Contents

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2007	2006	2007	2006
Net revenues from research collaborators	\$ 9,133	\$ 6,021	\$ 16,350	\$ 11,738
<b>Operating expenses:</b>				
Research and development <sup>(1)</sup>	18,813	12,599	45,484	24,306
General and administrative <sup>(1)</sup>	5,273	4,531	9,813	8,338
Total operating expenses	24,086	17,130	55,297	32,644
Loss from operations	(14,953)	(11,109)	(38,947)	(20,906)
<b>Other income (expense):</b>				
Interest income	2,578	1,538	5,268	2,798
Interest expense	(275)	(230)	(561)	(468)
Other expense	(41)	(109)	(96)	(194)
Total other income (expense)	2,262	1,199	4,611	2,136
Net loss	\$ (12,691)	\$ (9,910)	\$ (34,336)	\$ (18,770)
Net loss per common share basic and diluted	\$ (0.34)	\$ (0.31)	\$ (0.92)	\$ (0.60)
Weighted average common shares basic and diluted	37,534	32,010	37,454	31,080
<b>Comprehensive loss:</b>				
Net loss	\$ (12,691)	\$ (9,910)	\$ (34,336)	\$ (18,770)
Foreign currency translation adjustments	28	158	82	229
Unrealized (loss) gain on marketable securities	(94)	26	(165)	25
Comprehensive loss	\$ (12,757)	\$ (9,726)	\$ (34,419)	\$ (18,516)
(1) Non-cash stock-based compensation expense included in these amounts are as follows:				
Research and development	\$ 864	\$ 918	\$ 2,020	\$ 2,448

Edgar Filing: ALNYLAM PHARMACEUTICALS, INC. - Form 10-Q

General and administrative	922	688	1,926	1,533
The accompanying notes are an integral part of these condensed consolidated financial statements.				
2				

---

**Table of Contents**

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

	<b>Six Months Ended June 30,</b>	
	<b>2007</b>	<b>2006</b>
<b>Cash flows from operating activities:</b>		
Net loss	\$ (34,336)	\$ (18,770)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	2,132	877
Non-cash stock-based compensation	3,946	3,981
Non-cash license expense	7,909	130
Charge for 401(k) company stock match	139	45
Changes in operating assets and liabilities:		
Proceeds from landlord for tenant improvements	295	1,106
Collaboration receivables	(1,785)	(2,982)
Prepaid expenses and other assets	186	(313)
Accounts payable	1,583	1,712
Accrued expenses	5,494	727
Deferred revenue	(4,984)	(4,548)
Deferred rent	69	950
Net cash used in operating activities	(19,352)	(17,085)
<b>Cash flows from investing activities:</b>		
Purchases of property and equipment	(2,849)	(3,949)
Purchases of marketable securities	(128,691)	(62,647)
Sales of marketable securities	107,692	39,270
Net cash used in investing activities	(23,848)	(27,326)
<b>Cash flows from financing activities:</b>		
Proceeds from issuance of common stock, net of issuance costs	519	62,659
Proceeds from notes payable	957	2,582
Repayments of notes payable	(1,569)	(923)
Net cash (used in) provided by financing activities	(93)	64,318
Effect of exchange rate on cash	(198)	(19)
Net (decrease) increase in cash and cash equivalents	(43,491)	19,888
Cash and cash equivalents, beginning of period	127,955	15,757
Cash and cash equivalents, end of period	\$ 84,464	\$ 35,645

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



Table of Contents

**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 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 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 stock 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 stock excluded from the calculation of net loss per share because their inclusion would be anti-dilutive:

	<b>Three Months Ended June 30,</b>		<b>Six Months Ended June 30,</b>	
	<b>2007</b>	<b>2006</b>	<b>2007</b>	<b>2006</b>
Options to purchase common stock	4,782,032	3,865,388	4,782,032	3,865,388
Unvested restricted common stock		2,956		2,956
Common stock issued in connection with				
Garching agreements		8,594		8,594
Options that were exercised before				
vesting	13,941	44,454	16,941	48,404
	4,795,973	3,921,392	4,798,973	3,925,342



**Table of Contents*****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 improving disclosures about those measures. The standard is 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 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. 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 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 approximately \$4.2 million from Oxford pursuant to the agreement. Of such amount, approximately \$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, approximately \$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 approximately \$1.0 million from Oxford pursuant to the agreement. Of such amount, approximately \$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, approximately \$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 June 30, 2007, there was \$4.0 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%, maturing 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 paid principal and interest, 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 June 30, 2007, there was \$4.5 million outstanding under this line of credit with Lighthouse.

**Table of Contents**

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

Remainder of 2007	\$ 2,134
2008	4,268
2009	3,513
2010	480
2011	80
Total through 2011	10,475
Less: portion representing interest	1,952
Principal	8,523
Less: current portion	3,617
Long-term notes payable	\$ 4,906

**3. SIGNIFICANT AGREEMENTS*****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 approximately \$58.5 million. Novartis owned approximately 14% of the Company's outstanding common stock at June 30, 2007.

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 RNA interference (*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 from 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.



## **Table of Contents**

### ***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.

### ***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 amends and restates 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 is focused on developing RNAi therapeutics for targets associated with human diseases. The Amended License Agreement originally contemplated that Merck would focus on the nine targets that then remained to be nominated by Merck under the terms of the Original License Agreement. However, Merck and the Company agreed that Merck would cease working on four such targets while Merck's rights to two targets remain in place. The Amended License Agreement contemplates that Merck will name three additional targets for development and that the Company may select one as a joint development program, which Merck will co-fund and participate in from the outset. These programs will be in addition to the existing program directed to the NOGO pathway on which the Company and Merck are already collaborating. The Company may select three of the nine additional programs as joint development programs, which Merck will co-fund and participate in from the outset, two of which have been selected and comprise the two remaining active programs under the Amended License Agreement. To date, the Company has selected two co-development programs from the first six targets presented by Merck under the Amended License Agreement. The Amended License Agreement provides for funding from Merck immediately for programs selected by the Company for co-development, and provides that, in the United States, the Company will have the right to co-promote RNAi therapeutic products developed in these three co-development programs. Merck will assume primary responsibility for the remaining two programs and the Company is eligible to receive milestone payments and royalties on any RNAi therapeutic products developed and commercialized by Merck in these two programs.

The Company is recognizing the remaining deferred revenue on a straight-line basis over the remaining period of expected performance of four years, which ends in 2011.

### ***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 will focus 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.

### ***NIH Contract***

In September 2006, the Company was awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic against 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

will 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

## **Table of Contents**

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.

### **4. TEKmira PHARMACEUTICALS CORPORATION**

In January 2007, Inex Pharmaceuticals, Inc., now known as Tekmira Pharmaceuticals Corporation ( Tekmira ), granted the Company an exclusive license to its liposomal delivery formulation technology for the discovery, development and commercialization of RNAi therapeutics. The Company granted Tekmira an option for three InterfeRx licenses, subject to the Company's review and third party obligations to develop its own RNAi therapeutic products and exclusive access to certain intellectual property to develop oligonucleotide drugs that do not function through an RNAi mechanism.

In connection with Tekmira's license grant, the Company issued Tekmira 361,990 shares of common stock in a private placement in January 2007, which was valued at \$7.9 million, and in February 2007, paid Tekmira an additional \$0.4 million. The Company has also 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. In addition, the Company will be required to pay Tekmira \$13.0 million in milestone payments for each product that the Company develops utilizing technology Tekmira has licensed to the Company.

### **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 June 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 \$54.6 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 \$2.3 million and \$1.7 million, respectively, available to reduce future tax liabilities, and, which 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 commenced studies to assess the impact of change of control and the amount of usable research and development credits. Any limitation may result in expiration of a portion of the NOL or research and development credit carryforwards before utilization. Further, until the studies are completed and any limitations are known, no amounts are being presented as an uncertain tax position under FIN 48.

Through June 30, 2007, the Company has always generated operating losses and, as a result, has not recorded a tax provision and recorded a full valuation allowance against its net deferred tax assets. The proceeds from the Roche agreements (see Note 6) are expected to cause the Company to realize its deferred tax assets and, as a result, the Company expects to release the valuation allowance against its net deferred tax assets in the third quarter of 2007. At December 31, 2006, the valuation allowance was \$50.9 million but the amount of valuation allowance that will be released will depend upon several factors, including: the amount of losses and tax credits incurred through June 30, 2007; the results of the ongoing research and development credit study and Section 382 study that will determine the amount of usable research and development credits and net operating loss carryforwards; and, analysis of its deferred



tax assets to determine the amount of benefits that relate to equity items, such as tax deductions resulting from stock option exercises, which would be credited to additional paid-in capital.

**Table of Contents**

**6. SUBSEQUENT EVENTS**

***Roche***

**License and Collaboration Agreement**

In July 2007, the Company and, for limited purposes, Alnylam Europe, a German stock corporation and a wholly owned subsidiary of Alnylam, entered into a License and Collaboration Agreement (the "LCA") with F. Hoffmann-La Roche Ltd, a Swiss corporation ("Roche Basel"), and Hoffman-La Roche Inc., a New Jersey corporation (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 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, which may be expanded to include other therapeutic areas under certain circumstances.

In consideration for the rights granted to Roche under the LCA, Roche is required to pay to 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, 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 or 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 connection with the LCA and the Common Stock Purchase Agreement, the Company expects to pay approximately \$30.0 million to certain entities from which the Company licenses certain intellectual property in accordance with the applicable license agreements with these parties, primarily to Isis Pharmaceuticals, Inc.

**Common Stock Purchase Agreement**

In July 2007, the Company executed a Common Stock Purchase Agreement (the "Common Stock Purchase Agreement") with Roche Finance Ltd, a Swiss corporation and an affiliate of Roche ("Roche Finance"), which became effective in August 2007. Under the terms of the Common Stock Purchase Agreement, Roche Finance purchased 1.975 million shares of common stock, \$0.01 par value per share, of the Company (the "Shares"), for an aggregate purchase price of \$42.5 million.

Under the terms of the Common Stock Purchase Agreement, in the event the Company proposes to sell or issue any equity securities of the Company, other than securities issued pursuant to compensation plans and other specified exceptions, the Company agreed to grant to Roche Finance the right to acquire, at the then fair market value, a number of additional securities, of the same type as those issued, based on the percentage of outstanding shares of the Company's common stock then owned by Roche Finance. Roche Finance agreed, for a period of three years following the closing of the transactions contemplated by the Common Stock Purchase Agreement, neither it nor any specified affiliates of Roche Finance that are controlled by Roche Holdings Ltd will acquire any of the Company's securities or assets (other than an acquisition resulting in such entities beneficially owning less than 5% of the total outstanding voting securities of the Company), participate in any tender or exchange offer, merger or other business combination involving the Company or seek to control the management, Board of Directors or policies of the Company, subject to specified exceptions. Roche Finance also agreed that neither it nor any specified affiliates of Roche Finance that are controlled by Roche Holdings Ltd will sell or transfer any equity securities of the Company during the two-year

period following the closing of the transactions contemplated by the Common Stock Purchase Agreement and will limit the volume of such sales or transfers in a single

## **Table of Contents**

day during the following one-year period, in each case, for so long as Roche Finance and such affiliates beneficially own more than 2.5% of the total outstanding shares of the Company's common stock.

### **Share Purchase Agreement**

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, a German limited liability company and 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 agreed to create a new, wholly owned German limited liability company ("Roche Kulmbach"), into which substantially all of the non-intellectual property assets of Alnylam Europe shall be transferred, and Roche Germany agreed to purchase from the Company all of the issued and outstanding shares of Roche Kulmbach, for an aggregate purchase price of \$15.0 million.

### ***Amended and Restated Collaboration Agreement with Medtronic***

In July 2007, the Company and Medtronic, Inc. ("Medtronic") entered into an amended and restated collaboration agreement ("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 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 are, more traditional pharmaceutical royalties, intended to reflect each parties' contribution.

After the fulfillment of a specified initial commitment obligation, each party has the right to opt out of continued funding of the program and, if Medtronic opts out of the program, the Company may elect to commercialize and pay Medtronic royalties on net sales of any products developed in the program. Following the exercise by a party of its right to opt out of the program, the commercializing party will pay royalties at a reduced level based on the last specified program milestone to have been achieved before the other party opted 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 provide for 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 breaches 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.

***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 against hemorrhagic fever virus with the United States Department of Defense. The federal contract will provide

**Table of Contents**

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.

**Table of Contents****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, and 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, and 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, we are working on a number of programs including another viral respiratory infection, influenza, ALN-PCS01, an RNAi therapeutic targeting a gene called PCSK9 for the treatment of hypercholesterolemia, and ALN-VSP01, an RNAi therapeutic that is designed to target vascular endothelial growth factor, or VEGF, and kinesin spindle protein, or KSP, for the treatment of liver cancers and potentially other cancers. We have pre-clinical discovery programs focused on central nervous system, or CNS, diseases including Parkinson's disease, Huntington's disease, neuropathic pain, 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 a program for Ebola virus infection. We are also 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™, and are developing technology to achieve efficient and safe systemic delivery. 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, F. Hoffmann-La Roche Ltd, or Roche, Merck & Co., Inc., or Merck, Biogen Idec, Inc., or Biogen Idec, and Medtronic, Inc., or Medtronic.

We commenced operations in June 2002 and, since then, have focused our efforts primarily on business planning, research and development, acquiring intellectual property rights, recruiting management and technical staff and raising capital. Since our inception, we have generated significant losses. As of June 30, 2007, we had an accumulated deficit of \$174.9 million. Through June 30, 2007, we have funded our operations primarily through the net proceeds from the sale of equity securities and payments



## **Table of Contents**

under strategic alliances. Through June 30, 2007, a substantial portion of our total net revenues have been collaboration revenues derived from our strategic alliances with Novartis, Merck and the United States government related to hemorrhagic fever virus, including Ebola. We expect our revenues to continue to be derived primarily from strategic alliances, such as our collaborations with Novartis, Roche, Merck and Biogen Idec, the government for Ebola, other government and foundation funding and license fee revenues.

We currently have programs focused in a number of therapeutic areas. However, we are unable to predict when, if ever, we will be able to commence sales of any product. We have not and may never achieve profitability on a quarterly or annual basis and we expect to incur significant 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.

### ***Recent Developments***

In July 2007, we and, for limited purposes, Alnylam Europe, a German stock corporation and our wholly owned subsidiary, entered into a license and collaboration agreement, or LCA, with F. Hoffmann-La Roche Ltd, a Swiss corporation, or Roche Basel, and Hoffman-La Roche Inc., a New Jersey corporation, or 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 our intellectual property to develop and commercialize therapeutic products that function through RNAi, subject to our existing contractual obligations to third parties. The license is initially limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases and may be expanded to include other therapeutic areas under certain circumstances.

In consideration for the rights granted to Roche under the LCA, Roche is required to pay us \$273.5 million in upfront cash payments. Roche is also required to make payments to us 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, we have also agreed to collaborate with Roche on the discovery of RNAi therapeutic products directed to one or more disease targets, 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. In exchange for our contributions to the collaboration, Roche has agreed to make additional milestone and royalty payments.

In July 2007, we executed a common stock purchase agreement, or Common Stock Purchase Agreement, with Roche Finance Ltd, a Swiss corporation and an affiliate of Roche, or Roche Finance, which became effective in August 2007. Under the terms of the Common Stock Purchase Agreement, Roche Finance purchased 1.975 million shares of our common stock for an aggregate purchase price of \$42.5 million.

In connection with the LCA and the Common Stock Purchase Agreement, we expect to pay approximately \$30.0 million to certain entities from which we license certain intellectual property in accordance with the applicable license agreements with these parties, primarily to Isis.

In connection with the execution of the LCA and the Common Stock Purchase Agreement, we also executed a share purchase agreement, or Alnylam Europe Purchase Agreement with Alnylam Europe and Roche Beteiligungs GmbH, a German limited liability company and an affiliate of Roche Basel and Roche Finance, or Roche Germany. Under the terms of the Alnylam Europe Purchase Agreement which became effective in August 2007, we agreed to create a new, wholly owned German limited liability company, or Roche Kulmbach, into which substantially all of the non-intellectual property assets of Alnylam Europe shall be transferred, and Roche Germany agreed to purchase from us all of the issued and outstanding shares of Roche Kulmbach, for an aggregate purchase price of \$15.0 million.

### ***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. Included in our current programs are development programs, those programs for which we have established targeted timing for human clinical trials, and discovery programs, those programs for which we have yet to establish programs for targeted timing for human clinical trials. All of our programs are in the early stages of development. Our most advanced development program is focused on RSV, which began Phase II clinical trials in June 2007. Our other development programs are focused on another lung infection, influenza, or flu, the treatment of hypercholesterolemia and the treatment of liver cancers and potentially other 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, neuropathic pain; viral disease, such as Ebola; PML and several other diseases that are the subject of collaborations with Merck, Medtronic and Novartis, 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 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;

**Table of Contents**

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 Pharmaceuticals, Inc., or 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) Merck to develop RNAi technology and therapeutics, (4) 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 (5) 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.

**Critical Accounting Policies and Estimates**

There have been no significant changes to our critical accounting policies since the beginning of this fiscal year. Our 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.

**Results of Operations**

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

	<b>Three Months Ended June</b>		<b>Six Months Ended June</b>	
	<b>30,</b>		<b>30,</b>	
	<b>2007</b>	<b>2006</b>	<b>2007</b>	<b>2006</b>
Net revenues from research collaborators	\$ 9,133	\$ 6,021	\$ 16,350	\$ 11,738
Operating expenses	24,086	17,130	55,297	32,644
Loss from operations	(14,953)	(11,109)	(38,947)	(20,906)
Net Loss	\$ (12,691)	\$ (9,910)	\$ (34,336)	\$ (18,770)

**Revenues**

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

**Table of Contents**

	<b>Three Months Ended June 30,</b>		<b>Six Months Ended June 30,</b>	
	<b>2007</b>	<b>2006</b>	<b>2007</b>	<b>2006</b>
Novartis	\$ 4,440	\$ 5,615	\$ 8,525	\$ 10,784
Other research collaborators	4,550	298	7,052	637
InterfeRx program, research reagent licenses and other	143	108	773	317
Total net revenues from research collaborators	\$ 9,133	\$ 6,021	\$ 16,350	\$ 11,738

The decrease in Novartis revenues in the three months ended June 30, 2007 compared to the three months ended June 30, 2006 was due to a decrease in the amount of resources allocated to the Novartis flu alliance. The decrease in Novartis revenues in the six months ended June 30, 2007 compared to the six months ended June 30, 2006 was due to a decrease in the amount of resources allocated to our Novartis flu alliance as well as lower external expense reimbursement under our Novartis flu alliance.

In the three and six months ended June 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 increase in InterfeRx program, research reagent licenses and other revenues for the six months ended June 30, 2007 compared to the six months ended June 30, 2006 was due to the achievement of milestones pursuant to license agreements entered into under our InterfeRx program as well as an increase in research reagent licenses revenues as compared to the prior year.

Total deferred revenue of \$12.9 million at June 30, 2007 consists of payments received from collaborators pursuant to license agreements that we have yet to earn pursuant to our revenue recognition policy.

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

**Operating expenses**

The following table summarizes our operating expenses for the periods indicated, in thousands:

	<b>Three Months Ended June 30, 2007</b>	<b>% of Total Operating Expenses</b>	<b>Three Months Ended June 30, 2006</b>	<b>% of Total Operating Expenses</b>	<b>Increase</b>	
					<b>\$</b>	<b>%</b>
Research and development	\$ 18,813	78%	\$ 12,599	74%	\$ 6,214	49%
General and administrative	5,273	22%	4,531	26%	742	16%
Total operating expenses	\$ 24,086	100%	\$ 17,130	100%	\$ 6,956	41%

**Table of Contents**

	Six Months Ended June 30, 2007	% of Total Operating Expenses	Six Months Ended June 30, 2006	% of Total Operating Expenses	Increase	
					\$	%
Research and development	\$ 45,484	82%	\$ 24,306	74%	\$ 21,178	87%
General and administrative	9,813	18%	8,338	26%	1,475	18%
Total operating expenses	\$ 55,297	100%	\$ 32,644	100%	\$ 22,653	69%

**Research and development**

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

	Three Months Ended June 30, 2007	% of Expense Category	Three Months Ended June 30, 2006	% of Expense Category	Increase (Decrease)	
					\$	%
<b>Research and development</b>						
External services	\$ 5,686	30%	\$ 856	7%	\$ 4,830	564%
Clinical trial and manufacturing expenses	4,764	25%	4,138	33%	626	15%
Compensation related	3,306	18%	2,543	20%	763	30%
Facilities-related expenses	2,138	11%	1,500	12%	638	43%
Lab supplies and materials	1,416	8%	1,533	12%	(117)	(8%)
Non-cash stock-based compensation	864	5%	918	7%	(54)	(6%)
License fees	93	1%	767	6%	(674)	(88%)
Other	546	2%	344	3%	202	59%
<b>Total research and development</b>	<b>\$ 18,813</b>	<b>100%</b>	<b>\$ 12,599</b>	<b>100%</b>	<b>\$ 6,214</b>	<b>49%</b>

As indicated in the table above, the increase in research and development expenses in the three months ended June 30, 2007 as compared to the three months ended June 30, 2006 was primarily due to an increase in external service costs associated with our pre-clinical programs for the treatment of hypercholesterolemia, liver cancer and Ebola as well as higher expenses associated with our delivery related collaborations. The increase was also due to an increase in clinical trial expenses in support of our clinical program for RSV, which recently began Phase II trials, as well as costs related to an increase in research and development headcount over the past year to support our expanding pipeline and alliances. We expect to continue to devote a substantial portion of our resources to research and development expenses and that research and development expenses will increase as we continue development of our and our collaborators' product candidates and technologies. In connection with the Roche alliance, we expect to incur approximately \$30.0 million of license fees related to payments to certain entities from which we license certain

intellectual property in accordance with the applicable license agreements with these parties, primarily to Isis.

**Table of Contents**

	Six Months Ended June 30, 2007	% of Expense Category	Six Months Ended June 30, 2006	% of Expense Category	Increase (Decrease) \$	%
<b>Research and development</b>						
Clinical trial and manufacturing expenses	\$ 11,424	25%	\$ 6,439	26%	\$ 4,985	77%
License fees	8,636	19%	1,126	5%	7,510	667%
External services	8,079	18%	2,825	12%	5,254	186%
Compensation related	6,612	15%	4,880	20%	1,732	35%
Facilities-related expenses	4,204	9%	2,883	12%	1,321	46%
Lab supplies and materials	3,403	7%	2,946	12%	457	16%
Non-cash stock-based compensation	2,020	4%	2,448	10%	(428)	(17%)
Other	1,106	3%	759	3%	347	46%
<b>Total research and development</b>	<b>\$ 45,484</b>	<b>100%</b>	<b>\$ 24,306</b>	<b>100%</b>	<b>\$ 21,178</b>	<b>87%</b>

As indicated in the table above, the increase in research and development expenses in the six months ended June 30, 2007 as compared to the six months ended June 30, 2006 was primarily due to an increase in license fees, including a non-cash license fee of \$7.9 million and a cash license fee of \$0.4 million related to the issuance of our stock to Tekmira during the first quarter of 2007 in exchange for the worldwide exclusive license to Tekmira's liposomal delivery formulation technology for the discovery, development, and commercialization of RNAi therapeutics, as well as the expansion of the technology research and manufacturing alliance on lipid-based delivery technology. 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.

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.

**General and administrative**

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

Three Months Ended	% of Expense	Three Months Ended	% of Expense	Increase (Decrease)
--------------------------	-----------------	--------------------------	-----------------	------------------------

	June 30, 2007	Category	June 30, 2006	Category	\$	%
<b>General and administrative</b>						
Consulting and professional services	\$ 2,126	40%	\$ 1,538	34%	\$ 588	38%
Compensation related	1,092	21%	845	19%	247	29%
Non-cash stock-based compensation	922	17%	688	15%	234	34%
		17				

---



**Table of Contents**

	<b>Three Months Ended June 30, 2007</b>	<b>% of Expense  Category</b>	<b>Three Months Ended June 30, 2006</b>	<b>% of Expense  Category</b>	<b>Increase (Decrease)</b>	
					<b>\$</b>	<b>%</b>
Facilities related	587	11%	671	15%	(84)	(13%)
Insurance	152	3%	155	3%	(3)	(2%)
Other	394	8%	634	14%	(240)	(38%)
<b>Total general and administrative</b>	<b>\$ 5,273</b>	<b>100%</b>	<b>\$ 4,531</b>	<b>100%</b>	<b>\$ 742</b>	<b>16%</b>

As indicated in the table above, the increase in general and administrative expenses during the three months ended June 30, 2007 as compared to the three months ended June 30, 2006 was primarily due to higher professional service fees, which were the result of increased business development activities, including our alliance with Roche, which became effective in August 2007, as well as higher costs supporting overall corporate growth.

	<b>Six Months Ended June 30, 2007</b>	<b>% of Expense  Category</b>	<b>Six Months Ended June 30, 2006</b>	<b>% of Expense  Category</b>	<b>Increase (Decrease)</b>	
					<b>\$</b>	<b>%</b>
<b>General and administrative</b>						
Consulting and professional services	\$ 3,541	36%	\$ 2,719	33%	\$ 822	30%
Compensation related	2,088	21%	1,688	20%	400	24%
Non-cash stock-based compensation	1,926	20%	1,533	18%	393	26%
Facilities related	1,025	10%	1,258	15%	(233)	(19%)
Insurance	328	3%	317	4%	11	3%
Other	905	10%	823	10%	82	10%
<b>Total general and administrative</b>	<b>\$ 9,813</b>	<b>100%</b>	<b>\$ 8,338</b>	<b>100%</b>	<b>\$ 1,475</b>	<b>18%</b>

As indicated in the table above, the increase in general and administrative expenses during the three months ended June 30, 2007 as compared to the three months ended June 30, 2006 was primarily due to higher professional service fees, which were the result of increased business development activities, including our alliance with Roche, which became effective in August 2007, as well as higher costs supporting overall corporate growth.

**Interest income, interest expense and other**

Interest income was \$2.6 million and \$5.3 million for the three and six months ended June 30, 2007, respectively, compared to \$1.5 million and \$2.8 million for the three and six months ended June 30, 2006, respectively. The increase in both periods was due to our higher average cash, cash equivalent and marketable securities balances due primarily to proceeds we received from our December 2006 public offering of common stock.

Interest expense was \$0.3 million and \$0.6 million for the three and six months ended June 30, 2007, respectively, compared to \$0.2 million and \$0.5 million for the three and six months ended June 30, 2006,

respectively. Interest expense in each year related to borrowings under our lines of credit used to finance capital equipment purchases.

### **Liquidity and Capital Resources**

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

	<b>Six Months Ended June 30,</b>	
	<b>2007</b>	<b>2006</b>
Net loss	\$ (34,336)	\$ (18,770)
Adjustments to reconcile net loss to net cash used in operating activities	14,126	5,033
Changes in operating assets and liabilities	858	(3,348)
Net cash used in operating activities	(19,352)	(17,085)
Net cash used in investing activities	(23,848)	(27,326)

**Table of Contents**

	<b>Six Months Ended June 30,</b>	
	<b>2007</b>	<b>2006</b>
Net cash (used in) provided by financing activities	(93)	64,318
Effect of exchange rate on cash	(198)	(19)
Net (decrease) increase in cash and cash equivalents	(43,491)	19,888
Cash and cash equivalents, beginning of period	127,955	15,757
Cash and cash equivalents, end of period	\$ 84,464	\$ 35,645

Since we commenced operations in June 2002, we have generated significant losses. At June 30, 2007, we had an accumulated deficit of \$174.9 million. At June 30, 2007, we had cash, cash equivalents and marketable securities of \$194.8 million, compared to cash, cash equivalents and marketable securities of \$217.3 million at December 31, 2006. 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. This trend continued in the six months ended June 30, 2007 as our use of cash in our operating activities increased as compared to the six months ended June 30, 2006. The main components of our use of cash in operating activities are 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 accrued expenses of \$5.5 million for the six months ended June 30, 2007. Additionally, net accounts receivable increased \$1.8 million and deferred revenue increased \$5.0 million for the six months ended June 30, 2007. Our cash utilization is expected to continue for the remainder of 2007 and thereafter 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 six months ended June 30, 2007, net cash used in investing activities of \$23.8 million resulted from net purchases of marketable securities of \$21.0 million as well as purchases of property and equipment of \$2.8 million. For the six months ended June 30, 2006, net cash used in investing activities resulted from net purchases of marketable securities of \$23.4 million, as well as purchases of property and equipment of \$3.9 million.

***Financing activities***

For the six months ended June 30, 2007, net cash used in financing activities was \$0.1 million compared to \$64.3 million of net cash provided by financing activities for the six months ended June 30, 2006. The change in net cash provided by financing activities was due primarily to the net proceeds of \$62.2 million from our follow-on public offering in January 2006.

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%, maturing 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 June 30, 2005, at which point all draw-downs began to be repaid over 48 months. On the maturity of each equipment advance

## **Table of Contents**

under the line of credit, we are required to pay, in addition to the paid principal and interest, 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 June 30, 2007, we had an aggregate outstanding balance of \$8.5 million under all our loan agreements and \$1.9 million available under our equipment line of credit with Oxford.

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. Under the terms of the Roche alliance, Roche has agreed to pay us \$331.0 million in upfront cash payments and an equity investment, which will be partially offset by approximately \$30.0 million that we are required to pay to certain entities from which we license certain intellectual property in accordance with the applicable license agreements with these parties, primarily Isis. 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 collaborative arrangements and public or private financings. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our existing stockholders may result. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue.

Even if we are able to raise additional funds in a timely manner, our future capital requirements may vary from what we expect and will depend on many factors, including 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; 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 have 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. Related to the Roche alliance, we will have to pay approximately \$30.0 million to certain entities from which we license certain intellectual property in accordance with the applicable license agreements with these parties, primarily Isis. 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. There have been no other material changes in our contractual obligations and commitments since December 31, 2006.

**Table of Contents**

**Recently Issued Accounting Pronouncements**

In September 2006, the Financial Accounting Standards Board, or 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 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 June 2007, the FASB reached a consensus on EITF 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.

**Table of Contents**

**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 June 30, 2007 would impact the net fair value of such interest-sensitive financial instruments by approximately \$0.6 million.

***Foreign Currency Exchange Rate Risk***

We are exposed to foreign currency exchange rate risk. Our European operations are based in Kulmbach, Germany and the functional currency of these operations is the Euro. We provide funding to our European operations to pay for obligations denominated in Euros. The effect that fluctuations in the exchange rate between the Euro and the United States Dollar have on the amounts payable to fund our European operations are recorded in our consolidated statements of operations as other income or expense. We do not enter into any foreign exchange hedge contracts.

Assuming the amount of expenditures by our European operations were consistent with 2006 and the timing of the funding of these operations were to remain consistent during the remainder of 2007, a constant increase or decrease in the exchange rate between the Euro and the United States Dollar during the remainder of 2007 of 10% would result in a foreign exchange gain or loss of approximately \$0.1 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 June 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 June 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 June 30, 2007 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.



**Table of Contents**

**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 June 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 and commercialization of our products;

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, 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. There are also potential 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.

Very 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



## **Table of Contents**

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 June 30, 2007, we had an accumulated deficit of \$174.9 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;

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;

## **Table of Contents**

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. While the exercise of this right may provide us with additional funding under some circumstances, Novartis' exercise of this right 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 after two years under some circumstances or 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 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. 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

## Table of Contents

with respect to such targets. This right of first offer may make it difficult for us to form future alliances with other parties, which could impair development of our own products. If we are unable to develop products independent of Novartis, our business could be adversely affected.

***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 entered 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 Merck, 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. ***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



## **Table of Contents**

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 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.

***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 against 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 against 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 against 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.

***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 may also depend upon the use of specialized formulations, such as liposomes, whose scale-up and manufacturing could also 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 RNAi. We currently rely on several contract manufacturers for our supply of synthetic RNAi. 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, both of which could result in unusable product and cause delays in our development process. In addition, to fulfill our RNAi requirements we may need to secure alternative suppliers of

## **Table of Contents**

synthetic RNAi. The manufacturing process for any products that we may develop is an element of the FDA approval process and we will need to contract with manufacturers who can meet all applicable FDA 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.

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.***



## **Table of Contents**

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 to approximately 140 full time equivalent employees as of June 30, 2007, with offices and laboratory space in both Cambridge, Massachusetts and Kulmbach, Germany. In connection with our license and collaboration agreement with Roche, we sold to Roche our operations in Kulmbach, Germany, and after a transition period, 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. In addition, we need to find sufficient physical space to support that increase in our operations. Any failure to successfully rebuild the operations that were formerly performed in Kulmbach could have a material adverse effect on our business.

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 in at least two different countries. 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,

## **Table of Contents**

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;

- 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.

***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 any product candidate 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.



## **Table of Contents**

### ***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.

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;

**Table of Contents**

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.

***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;

32

---

**Table of Contents**

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 or hemorrhagic fever virus infection, 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 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

## **Table of Contents**

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;

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



## **Table of Contents**

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.***

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;

35

---

**Table of Contents**

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;

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, Nantech, Calando, 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 is currently one of our collaborators and a licensee under our intellectual property for specified disease targets. However, as a result of its acquisition of Sirna in December 2006, Merck, which has substantially more resources and experience in developing drugs than we do, could 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.

## **Table of Contents**

We also compete with companies working to develop antisense-based drugs. Like RNAi product candidates, antisense drugs target 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, and another company, Genta Inc., has an antisense drug candidate in late-stage 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.

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 Isis, Idera Pharmaceuticals, Inc., Carnegie Institution of Washington, Cancer Research Technology Limited, the Massachusetts Institute of Technology, the

Whitehead Institute for Biomedical Research, Max Planck Innovation, Stanford University, Cold Spring Harbor Laboratory, the University of South Alabama, CBR Institute for Biomedical Research, University of British Columbia 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

## **Table of Contents**

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. These applications claim many different methods, compositions and processes relating to the discovery, development and commercialization of RNAi therapeutics. Because the field is so new, very few of these patent applications have been fully processed by government patent offices around the world, and there is a great deal of 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 June 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 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 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.

In addition, there are many issued and pending patents that claim aspects of oligonucleotide chemistry that we may need to apply to our siRNA drug candidates. There are also many issued patents that claim 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



## **Table of Contents**

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

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

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

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

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

### **Risks Related to 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

## **Table of Contents**

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 14% of our outstanding common stock as of June 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

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

Our annual meeting of stockholders was held on June 1, 2007. At the annual meeting, the following matters were voted upon:

Our stockholders elected the two persons listed below as Class III directors, each to serve until our 2010 annual meeting of stockholders and until their successors are duly elected and qualified. The table set forth below lists the number of shares of our common stock voted in favor of the election of each such person, as well as the number of votes withheld for the election of such person:

	Number of Shares For	Number of Shares Withheld
Victor J. Dzau, M.D.	30,239,652	228,170

Kevin P. Starr

29,367,599

1,100,223

The terms of office of the following directors continued after the annual meeting:

40

---

**Table of Contents**

John K. Clarke

John M. Maraganore, Ph.D.

Vicki L. Sato, Ph.D.

Paul R. Schimmel, Ph.D.

Phillip A. Sharp, Ph.D.

James L. Vincent

Our stockholders ratified the appointment by our board of directors of PricewaterhouseCoopers L.L.P. as our independent auditors for the fiscal year ending December 31, 2007. The holders of 30,388,606 shares of our common stock voted in favor of this proposal. The holders of 57,947 shares voted against this proposal. The holders of 21,269 shares abstained from voting on this matter.

**ITEM 6. EXHIBITS**

- 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.

**Table of Contents**

**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: August 9, 2007

By: /s/ John M. Maraganore

John M. Maraganore, Ph.D.  
President and Chief Executive Officer  
(Principal Executive Officer)

Date: August 9, 2007

By: /s/ Patricia L. Allen

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

42