

ALNYLAM PHARMACEUTICALS, INC.

Form 10-Q

November 09, 2006

**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 September 30, 2006**

**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  
(Address of principal executive  
offices)

02142

(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 October 31, 2006, the registrant had 32,224,739 shares of Common Stock, \$0.01 par value per share, outstanding.

**Table of Contents**

	<b>INDEX</b>
	<b>PAGE</b>
	<b>NUMBER</b>
<b>PART I. FINANCIAL INFORMATION</b>	
ITEM 1. FINANCIAL STATEMENTS (Unaudited)	
<u>CONDENSED CONSOLIDATED BALANCE SHEETS AS OF SEPTEMBER 30, 2006 AND DECEMBER 31, 2005</u>	1
<u>CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS FOR THE THREE AND NINE MONTHS ENDED SEPTEMBER 30, 2006 AND 2005</u>	2
<u>CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS FOR THE NINE MONTHS ENDED SEPTEMBER 30, 2006 AND 2005</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>	13
<u>ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK</u>	24
<u>ITEM 4. CONTROLS AND PROCEDURES</u>	24
<b>PART II. OTHER INFORMATION</b>	
<u>ITEM 1A. RISK FACTORS</u>	25
<u>ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS</u>	44
<u>ITEM 6. EXHIBITS</u>	44
<u>SIGNATURES</u>	46
<u>Ex-10.1 Collaboration and License Agreement by and between the Registrant and Biogen Idec MA, Inc. dated September 20, 2006</u>	
<u>Ex-10.2 Letter Agreement by and between the Registrant and Vincent J. Miles effective as of October 20, 2006</u>	
<u>Ex-31.1 Section 302 Certification of CEO</u>	
<u>Ex-31.2 Section 302 Certification of CFO</u>	
<u>Ex-32.1 Section 906 Certification of CEO</u>	
<u>Ex-32.2 Section 906 Certification of CFO</u>	

**Table of Contents**

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

	<b>September 30, 2006</b>	<b>December 31, 2005</b>
<b>ASSETS</b>		
<b>Current assets:</b>		
Cash and cash equivalents	\$ 35,516	\$ 15,757
Marketable securities	84,758	64,245
Collaboration receivables	4,847	609
Related party notes receivable		146
Prepaid expenses and other current assets	1,706	1,657
Total current assets	126,827	82,414
Property and equipment, net of accumulated depreciation of \$7,732 and \$5,097 at September 30, 2006 and December 31, 2005, respectively	12,856	10,580
Intangible assets, net of accumulated amortization of \$1,454 and \$1,143 at September 30, 2006 and December 31, 2005, respectively	2,180	2,491
Restricted cash	2,313	2,313
Other assets	351	550
Total assets	\$ 144,527	\$ 98,348
 <b>LIABILITIES AND STOCKHOLDERS EQUITY</b>		
<b>Current liabilities:</b>		
Accounts payable	\$ 2,456	\$ 1,975
Accrued expenses	5,104	3,899
Current portion of notes payable	3,046	1,876
Deferred revenue	10,924	10,734
Total current liabilities	21,530	18,484
Deferred revenue, net of current portion	8,473	10,099
Deferred rent	3,310	2,467
Notes payable, net of current portion	6,437	5,519
Total liabilities	39,750	36,569
 <b>Stockholders equity:</b>		
Preferred stock, \$0.01 par value, 5,000,000 shares authorized and no shares issued and outstanding as of September 30, 2006 and December 31, 2005		
Common stock, \$0.01 par value, 125,000,000 shares authorized; 32,176,921 shares issued and outstanding as of September 30, 2006; 26,721,149 shares issued and 26,638,255 shares outstanding as of December 31, 2005	322	267
Additional paid-in capital	236,416	170,033

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

Deferred stock compensation	(135)	(2,460)
Accumulated other comprehensive gain (loss)	263	(142)
Accumulated deficit	(132,089)	(105,919)
Total stockholders' equity	104,777	61,779
Total liabilities and stockholders' equity	\$ 144,527	\$ 98,348

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)

	<b>Three Months Ended</b>		<b>Nine Months Ended</b>	
	<b>September 30,</b>		<b>September 30,</b>	
	<b>2006</b>	<b>2005</b>	<b>2006</b>	<b>2005</b>
<b>Net revenues</b>	\$ 8,211	\$ 1,413	\$ 19,949	\$ 4,164
 <b>Cost and expenses:</b>				
Research and development <sup>(1)</sup>	12,833	7,995	37,455	22,557
General and administrative <sup>(1)</sup>	3,982	4,088	12,004	10,162
Total costs and expenses	16,815	12,083	49,459	32,719
Loss from operations	(8,604)	(10,670)	(29,510)	(28,555)
 <b>Other income (expense):</b>				
Interest income	1,555	237	4,353	759
Interest expense	(265)	(244)	(733)	(717)
Other (expense) income	(86)	(1)	(280)	90
Total other income (expense)	1,204	(8)	3,340	132
Net loss	\$ (7,400)	\$ (10,678)	\$ (26,170)	\$ (28,423)
 Net loss per common share basic and diluted				
	\$ (0.23)	\$ (0.51)	\$ (0.83)	\$ (1.37)
 Weighted average common shares used to compute basic and diluted net loss per common share				
	32,122	20,914	31,465	20,674
 <b>Comprehensive loss:</b>				
Net loss	\$ (7,400)	\$ (10,678)	\$ (26,170)	\$ (28,423)
Foreign currency translation adjustments	47	(8)	276	(463)
Unrealized gain on marketable securities	104	9	129	11
Comprehensive loss	\$ (7,249)	\$ (10,677)	\$ (25,765)	\$ (28,875)

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

Research and development	\$	883	\$	1,074	\$	3,331	\$	1,815
General and administrative		831		1,122		2,364		1,780

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>Nine Months Ended September</b>	
	<b>30,</b>	
	<b>2006</b>	<b>2005</b>
<b>Cash flows from operating activities:</b>		
Net loss	\$ (26,170)	\$ (28,423)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	2,728	2,367
Non-cash stock-based compensation	5,695	3,595
Non-cash license expense	130	2,093
Charge for 401(k) company stock match	91	
Realized foreign currency losses (gains)	140	(90)
Changes in operating assets and liabilities:		
Proceeds from landlord for tenant improvements	1,106	
Collaboration receivables	(4,238)	548
Prepaid expenses and other assets	102	(330)
Accounts payable	469	1,088
Accrued expenses	1,252	(958)
Deferred revenue	(1,435)	9
Deferred tax asset	113	
Net cash used in operating activities	(20,017)	(20,101)
<b>Cash flows from investing activities:</b>		
Purchases of property and equipment	(4,695)	(1,347)
Purchases of marketable securities	(118,798)	(19,185)
Sales of marketable securities	98,286	27,328
Net cash (used in) provided by investing activities	(25,207)	6,796
<b>Cash flows from financing activities:</b>		
Proceeds from issuance of common stock, net of issuance costs	62,847	120
Proceeds from notes payable	3,613	762
Repayments of notes payable	(1,525)	(416)
Net cash provided by financing activities	64,935	466
Effect of exchange rate on cash	48	(255)
Net increase (decrease) in cash and cash equivalents	19,759	(13,094)
Cash and cash equivalents, beginning of period	15,757	20,272
Cash and cash equivalents, end of period	\$ 35,516	\$ 7,178

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**

**1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES**

***Basis of Presentation***

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 which 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, 2005, which were filed in the Company's Annual Report on Form 10-K with the Securities and Exchange Commission (the SEC) on March 16, 2006. 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.

***Principles of Consolidation***

The accompanying condensed consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiaries, Alnylam U.S., Inc. and Alnylam Europe AG. 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 of America requires management to make estimates and assumptions that affect (1) the reported amounts of assets and liabilities, (2) the disclosure of contingent assets and liabilities at the date of the financial statements and (3) the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

***Accounting for Stock-Based Compensation***

As of September 30, 2006, an aggregate of 5,520,662 shares of common stock were reserved for issuance under the Company's 2004 Stock Incentive Plan, including outstanding options to purchase 3,945,196 shares of common stock and 1,575,466 shares were available for future grant. Each option shall expire within ten years of issuance. Stock options granted by the Company to employees generally vest as to 25 percent of the shares on the first anniversary of the grant date and 6.25 percent of the shares at the end of each successive three-month period until fully vested. Since the Company's adoption of SFAS 123R, there have been no changes to the Company's equity plans or modifications to outstanding stock-based awards. Stock options granted by the Company to non-employee directors (1) upon their appointment to the board, vest as to one-third of such shares on each of the first, second and third anniversaries of the date of grant and (2) at each year's annual meeting at which they serve as a director, vest in full on the first anniversary of the date of grant.

In December 2004, the Financial Accounting Standards Board (FASB) issued Statement of Accounting Standard (SFAS) No. 123R, *Share-Based Payment, an amendment of FASB Statements Nos. 123 and 95* (SFAS 123R), that addresses the accounting for stock-based payment transactions in which a company receives employee services in exchange for either equity instruments of the company or liabilities that are based on the fair value of the company's equity instruments or that may be settled by the issuance of such equity instruments. The statement eliminates the ability to account for employee stock-based compensation transactions using the intrinsic method and requires that such transactions be accounted for using a fair-value-based method and recognized as expense on a straight-line basis over the vesting period in the consolidated statements of operations. In March 2005, the SEC issued Staff Accounting Bulletin (SAB) No. 107 (SAB 107) regarding the SEC staff's interpretation of SFAS 123R. This interpretation provides the SEC staff's views regarding interactions between SFAS 123R and certain SEC rules and regulations and provides interpretations of the valuation of stock-based payments for public companies. The interpretive guidance is intended to assist companies in applying the provisions of SFAS 123R and investors and users of the financial statements in analyzing the information provided.

**Table of Contents**

Effective January 1, 2006, the Company adopted the fair value recognition provisions of SFAS 123R using the modified- prospective-transition method. Under that transition method, stock-based compensation expense recognized for the nine months ended September 30, 2006 includes compensation for all stock-based payments granted prior to, but not yet vested as of, January 1, 2006, based on the grant date fair value estimated in accordance with the original provisions of SFAS No. 123, *Accounting for Stock-Based Compensation* ( SFAS 123 ), and compensation cost for all stock-based payments granted subsequent to January 1, 2006, based on the grant-date fair value estimated in accordance with the provisions of SFAS 123R. Such amounts have been reduced by the Company's estimate of forfeitures of all unvested awards. Results for prior periods have not been restated.

Prior to January 1, 2006, the Company accounted for its stock-based compensation plans under the recognition and measurement provisions of Accounting Principles Board ( APB ) Opinion No. 25, *Accounting for Stock Issued to Employees* ( APB 25 ), and related interpretations for all awards granted to employees. Under APB 25, when the exercise price of options granted to employees under these plans equals the market price of the common stock on the date of grant, no compensation expense is recorded. When the exercise price of options granted to employees under these plans is less than the market price of the common stock on the date of grant, compensation expense is recognized over the vesting period.

For stock options granted to non-employees, the Company recognizes compensation expense in accordance with the requirements of SFAS 123 and Emerging Issues Task Force Issue No. 96-18, *Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services* under which compensation expense is generally recognized over the vesting period of the award, which is generally the period during which services are rendered by such non-employees. Stock options granted by the Company to non-employees, other than members of our Board of Directors, generally vest over a four-year service period. The Company has two equity instruments that are required to be evaluated under SFAS 123R, stock option plans and an employee stock purchase plan.

Upon the adoption of SFAS 123R, \$0.8 million of the Company's deferred stock-based compensation balance of \$2.5 million as of December 31, 2005, which was accounted for under APB 25, was reclassified against additional paid-in-capital. The remaining portion of deferred stock-based compensation balance at September 30, 2006 was composed of \$0.1 million relating to the intrinsic value of stock options granted below fair market value that were accounted for under the minimum value method because the Company's stock was not publicly traded. The Company accounts for non-employee grants as an expense over the vesting period of the underlying stock options using the method prescribed by FASB Interpretation No. 28. At the end of each financial reporting period prior to vesting, the value of these options (as calculated using the Black-Scholes option-pricing model) is re-measured using the then-current fair value of the Company's common stock. The Company recognized approximately \$0.1 million and \$1.2 million of stock-based compensation expense related to these non-employee options for the three and nine months ended September 30, 2006,. Total compensation cost for all share-based payment arrangements for the three and nine months ended September 30, 2006 was \$1.7 million and \$5.7 million. Under the provisions of SFAS 123R, the Company recorded \$1.6 million and \$4.5 million of stock-based compensation for the three and nine months ended September 30, 2006, which represents an increase in basic and diluted net loss per share allocable to common stockholders of \$0.05 per share and \$0.14 per share for the three and nine months ended September 30, 2006. No amounts relating to the stock-based compensation have been capitalized.

The following table illustrates the effect on net loss and net loss per share if the Company had applied the fair value recognition provisions of SFAS 123 to options granted under the Company's stock option plans for the three and nine months ended September 30, 2005, in thousands, except per share amounts. For purposes of this pro-forma disclosure, the value of the options is estimated using a Black-Scholes option-pricing model and amortized to expense over the options' vesting periods.

**Table of Contents**

	<b>Three Months Ended September 30, 2005</b>	<b>Nine Months Ended September 30, 2005</b>
Net loss, as reported	\$ (10,678)	\$ (28,423)
Add: Total stock-based compensation expense determined under the intrinsic value method for all employee awards	1,154	2,110
Deduct: Total stock-based compensation expense determined under the fair value method for all employee awards	(2,463)	(4,275)
 Pro forma net loss	 \$ (11,987)	 \$ (30,588)
 Basic and diluted net loss per common share, as reported	 \$ (0.51)	 \$ (1.37)
Basic and diluted net loss per common share, pro forma	\$ (0.57)	\$ (1.48)

The fair value of stock options at date of grant, based on the following assumptions, was estimated using the Black-Scholes option-pricing model. The Company's expected stock-price volatility assumption is based on a combination of implied volatilities of similar entities whose share or option prices are publicly available as well as the historical volatility of our publicly traded stock. The expected life assumption is based on the simplified method provided for under SAB 107, which averages the contractual term of the Company's options (10 years) with the ordinary vesting term (2.2 years). The dividend yield assumption is based on the fact that the Company has never paid cash dividends and has no present intention to pay cash dividends. The risk-free interest rate used for each grant is equal to the zero coupon rate in effect at the time of grant for instruments with a similar expected life. Based on historical experience, the Company has assumed an annualized forfeiture rate of 4.35% for its stock options. The Company will record additional expense if the actual forfeitures are lower than estimated and will record a recovery of prior expense if the actual forfeitures are higher than estimated.

	<b>Three Months Ended September 30,</b>		<b>Nine Months Ended September 30,</b>	
	<b>2006</b>	<b>2005</b>	<b>2006</b>	<b>2005</b>
Risk-free interest rate	4.60%	3.82%	4.85%	3.75%
Expected dividend yield				
Expected option life	6.1 years	5 years	6 years	5 years
Expected volatility	67%	69%	67%	68%

As of September 30, 2006, there remained approximately \$7.5 million of unearned compensation expense related to unvested employee stock options to be recognized as expense over a weighted-average period of approximately 1.3 years.

**Table of Contents**

Presented below is the Company's stock option activity:

	Nine Months Ended			
	September 30, 2006		September 30, 2005	
	Number of Options	Weighted Average Exercise Price	Number of Options	Weighted Average Exercise Price
Outstanding at beginning of period	3,907,127	\$ 5.73	2,851,967	\$2.91
Granted	456,750	\$14.25	408,249	\$7.80
Exercised	(389,955)	\$ 1.78	(74,316)	\$0.67
Cancelled	(28,726)	\$ 6.87	(5,428)	\$4.92
Outstanding at end of period	3,945,196	\$ 7.10	3,180,472	\$3.58
Options exercisable at end of period	1,743,062	\$ 3.26	1,150,482	\$0.80
Weighted average fair value of options granted		\$ 9.21		\$4.28

The weighted average remaining contractual life for options outstanding and exercisable as of September 30, 2006 was 8.18 years and 7.41 years.

The aggregate intrinsic value of outstanding options as of September 30, 2006 was \$29.1 million, of which \$19.5 million related to exercisable options. The aggregate intrinsic value was calculated based on the positive difference between the closing fair market value of the Company's common stock on September 30, 2006 (\$14.41) and the exercise price of the underlying options. The intrinsic value of options exercised was \$0.3 million and \$39,000 for the three months ended September 30, 2006 and 2005. The intrinsic value of options exercised was \$5.2 million and \$0.5 million for the nine months ended September 30, 2006 and 2005.

**Employee Stock Purchase Plan**

In 2004, the Company adopted the 2004 Employee Stock Purchase Plan (the "2004 Purchase Plan") with 315,789 shares authorized for issuance. Under the 2004 Purchase Plan, the Company makes one offering each year, at the end of which employees may purchase shares of common stock through payroll deductions made over the term of the offering. The per-share purchase price at the end of the offering is equal to the lesser of 85% of the closing price of the common stock at the beginning or end of the offering period. The annual offering period begins on the 1st day of November each year and ends on the 31st day of October each year. The Company issued 51,792 shares during 2005 and as of September 30, 2006, 263,997 shares were available for issuance under the 2004 Purchase Plan. In connection with the 2006 annual offering period, the Company issued an additional 40,530 shares under the 2004 Purchase Plan on October 31, 2006.

The weighted average fair value of stock purchase rights granted as part of the 2004 Purchase Plan during the three and nine months ended September 30, 2006 was \$4.18. The fair value was estimated using the Black-Scholes option-pricing model. The Company used a weighted-average stock-price volatility of 70%, option life assumption of one year and risk-free rate of 4.18%. The Company recorded \$0.1 million of stock-based compensation for the nine months ended September 30, 2006 related to the 2004 Purchase Plan.

**401(k) Plan**

The Company maintains a 401(k) plan in which all of its regular employees in the United States are eligible to participate. Participants may contribute up to 60% of their annual base salary to the plan, subject to certain limitations. Beginning in April 2006, the Company began matching in common stock up to 3% of a participant's base salary. Employer common stock matches vest between immediately and two years, depending on years of service with the Company. Employees have the ability to transfer funds from the Company stock fund to other plan funds as they choose, subject to blackout periods. The Company issued 6,084 shares of common stock during the nine months

ended September 30, 2006 in connection with matches under the 401(k) plan.

**Table of Contents****Net Loss Per Common Share**

The Company accounts for and discloses net income (loss) per common share in accordance with 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), unvested restricted stock awards and the weighted average conversion of the preferred stock into shares of common stock (using the if-converted method) for periods prior to the Company's initial public offering, which was completed in June 2004. 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 September 30,</b>		<b>Nine Months Ended September 30,</b>	
	<b>2006</b>	<b>2005</b>	<b>2006</b>	<b>2005</b>
Options to purchase common stock	3,945,196	3,180,472	3,945,196	3,180,472
Warrants to purchase common stock		52,630		52,630
Unvested restricted common stock		118,037		118,037
Options that were exercised before vesting	36,403	68,744	44,345	76,909
	3,981,599	3,419,883	3,989,541	3,428,048

**Recent Accounting Pronouncements**

In July 2006, the FASB issued FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes* (FIN 48), which clarifies the accounting for uncertainty in income taxes recognized in a company's financial statements in accordance with FASB Statement No. 109, *Accounting for Income Taxes*. FIN 48 prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. This interpretation also provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure and transition. FIN 48 is effective for fiscal years beginning after December 15, 2006. The Company is currently assessing the impact, if any, of FIN 48 on its financial position and results of operations.

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measurements*. 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. The Company is currently evaluating the impact of SFAS No. 157 on its financial statements.

In September 2006, the U.S. Securities and Exchange Commission staff issued Staff Accounting Bulletin No. 108 (SAB 108), *Considering the Effects of Prior Year Misstatements when Quantifying Misstatements in Current Year Financial Statements*. SAB 108 eliminates the diversity of practice surrounding how public companies quantify financial statement misstatements. It establishes an approach that requires quantification of financial statement misstatements based on the effects of the misstatements on each of the company's financial statements and the related financial statement disclosures. SAB 108 must be applied to annual financial statements for their first fiscal year ending after November 15, 2006. The Company does not expect SAB 108 to have a material impact on its financial

condition or results of operations.



**Table of Contents****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 Company borrowed an aggregate of approximately \$388,000 from Oxford pursuant to the agreement. Of such amount, approximately \$241,000 bears interest at a fixed rate of 10.07% and is required to be repaid in 48 monthly installments of principal and interest beginning in March 2006. The remainder of such amount, approximately \$147,000, bears interest at a fixed rate of 10.09% and is required to be repaid in 36 monthly installments of principal and interest beginning in March 2006.

In June 2006, the Company borrowed an aggregate of approximately \$2.3 million from Oxford pursuant to the agreement. Of such amount, approximately \$2.1 million bears interest at a fixed rate of 10.37% and is required to be repaid in 36 monthly installments of principal and interest beginning in June 2006. The remainder of such amount, approximately \$0.2 million, bears interest at a fixed rate of 10.35% and is required to be repaid in 48 monthly installments of principal and interest beginning in June 2006.

In August 2006, the Company borrowed approximately \$1.1 million from Oxford pursuant to the agreement. Of such amount, approximately \$0.6 million bears interest at a fixed rate of 10.39% and is required to be repaid in 48 monthly installments of principal and interest beginning in August 2006. The remainder of such amount, approximately \$0.5 million, bears interest at a fixed rate of 10.41% and is required to be repaid in 36 monthly installments of principal and interest beginning in August 2006.

In March 2004, the Company entered into an agreement with Lighthouse Capital Partners V, L.P. ( Lighthouse ) to establish an equipment line of credit for \$10.0 million. In June 2005, the parties amended the agreement to allow the Company the ability to draw down amounts under the line of credit through December 31, 2005 upon adherence to certain conditions. 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. The Company was 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 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 September 30, 2006, there was \$6.0 million outstanding under this line of credit with Lighthouse.

In connection with the agreement, the Company issued to Lighthouse and an affiliate of Lighthouse warrants to purchase redeemable convertible preferred stock, which were converted into warrants to purchase 52,630 shares of the Company s common stock at an exercise price of \$9.50 per share upon the closing of the Company s initial public offering in June 2004. The Company recorded the fair value of these warrants of \$0.6 million as a deferred financing cost which is being amortized to interest expense over the 63-month repayment term of the first advance. The fair value of the warrants was calculated using the Black-Scholes option pricing model with the following assumptions: 100% volatility, risk-free interest rate of 3.49%, no dividend yield and a seven-year term. Lighthouse and its affiliate net-exercised these warrants in full during the second quarter of 2006 and the Company issued an aggregate of 18,072 shares in connection with such exercises.

As of September 30, 2006, future cash payments under the notes payable to Lighthouse and Oxford, including interest, are as follows, in thousands:

Remainder of 2006	\$ 953
2007	3,810
2008	3,810
2009	3,060
2010	162

Total through 2010	11,795
Less: portion representing interest	2,312
Principal	9,483
Less: current portion	3,046
Long-term notes payable	\$ 6,437

**Table of Contents****3. SIGNIFICANT AGREEMENTS*****Novartis Broad Alliance***

Beginning in September 2005, the Company entered into a series of transactions with Novartis. In September 2005, the Company and Novartis executed a stock purchase agreement (the *Stock Purchase Agreement*) and an investor rights agreement (the *Investor Rights Agreement*). In October 2005, in connection with the closing of the transactions contemplated by the *Stock Purchase Agreement*, the *Investor Rights Agreement* became effective and the Company and Novartis executed a research collaboration and license agreement (the *Collaboration and License Agreement*) (collectively the *Novartis Agreements*).

Under the terms of the *Stock Purchase Agreement*, on October 12, 2005, Novartis purchased 5,267,865 shares of the Company's common stock at a purchase price of \$11.11 per share for an aggregate purchase price of approximately \$58.5 million, which, after such issuance, represented 19.9% of the Company's outstanding common stock as of the date of issuance.

Under the terms of the *Investor Rights Agreement*, the Company granted Novartis demand and piggyback registration rights under the Securities Act of 1933, as amended, for the shares acquired by Novartis. The Company also granted to Novartis rights to acquire additional equity securities of the Company in the event that the Company proposes to sell or issue any equity securities of the Company, subject to specified exceptions, as described in the *Investor Rights Agreement*, such that Novartis would be able to maintain its ownership percentage in the Company. Novartis agreed, until the later of (1) three years from the date of the *Investor Rights Agreement* and (2) the date of termination or expiration of the *Selection Term* (as defined in the *Collaboration and License Agreement*), not to acquire any securities of the Company (other than an acquisition resulting in Novartis and its affiliates beneficially owning less than 20% 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 or influence the management, Board of Directors or policies of the Company, subject to specified exceptions described in the *Investor Rights Agreement*.

Under the terms of the *Collaboration and License Agreement*, the parties will work together on a defined number of selected targets, as defined in the *Collaboration and License Agreement*, to discover and develop therapeutics based on 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. In addition, Novartis may terminate the *Collaboration and License Agreement* after a period of two years under certain circumstances or in the event that the Company materially breaches its obligations. The Company may terminate the agreement with respect to particular programs, products and or countries in the event of certain material breaches of obligations by Novartis, or in its entirety under certain circumstances for multiple such breaches. Novartis made up-front payments totaling \$10.0 million to the Company in October 2005 in consideration for the rights granted to Novartis under the *Collaboration and License Agreement* and to reimburse prior costs incurred by the Company to develop *in vivo* RNAi technology. In addition, the *Collaboration and License Agreement* includes terms under which Novartis will provide the Company with research funding and milestone payments as well as royalties on annual net sales of products 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 terms of the *Collaboration and License Agreement* allow the Company to retain the right to discover, develop, commercialize or manufacture compounds that function through the mechanism of RNAi or products that contain such compounds as an active ingredient with respect to targets not selected by Novartis for inclusion in the *Collaboration and License Agreement*, provided that Novartis has a right of first offer in the event that the Company proposes to enter into an agreement with a third party with respect to any such target. The Company recognized \$5.5 million and \$14.3 million in revenues during the three and nine months ended September 30, 2006 and has \$10.2 million of deferred revenue on its balance sheet related to such agreements at September 30, 2006.

***Novartis Pandemic Flu Alliance***

In February 2006, the Company entered into a separate alliance with Novartis for the development of RNAi therapeutics for pandemic flu ( 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. Novartis will

**Table of Contents**

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 development efforts on RNAi therapeutics for pandemic flu, and to receive a significant share of any profits. The Company recognized \$1.0 million and \$2.9 million in revenues during the three and nine months ended September 30, 2006 under the Novartis Flu Agreement.

***Merck***

On July 3, 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). The collaboration between the Company and Merck is focused on developing RNAi therapeutics for targets associated with human diseases and, under the terms of the Amended License Agreement, will focus on the nine targets that remained to be nominated by Merck under the terms of the Original License Agreement. These nine 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. In October 2006, the Company selected a co-development program from the first three targets presented by Merck under the Amended License Agreement. Under the Original License Agreement, the collaboration was structured such that co-funding by Merck would not begin until after the completion of defined pre-clinical work. The Amended License Agreement provides 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 six programs and the Company is eligible to receive milestone payments and royalties on any RNAi therapeutic products developed and commercialized by Merck in these six programs. The initial term of the collaboration under the Amended License Agreement is five years from the date of the Original License Agreement and, unless earlier terminated, will continue until the date on which no product is being developed or commercialized under the agreement. Unless earlier terminated, the Amended License Agreement shall continue in effect until the expiration of all royalty obligations and profit-sharing obligations under the agreement.

On July 3, 2006, the Company and Merck agreed to terminate their Collaboration and License Agreement, effective as of June 29, 2004 (the Ocular Collaboration Agreement), pursuant to which the Company and Merck were collaborating in the research, development and commercialization of RNAi products directed to certain targets, including but not limited to, vascular endothelial growth factor (VEGF). In connection with the termination of the Ocular Collaboration Agreement, and subject to certain royalty and other obligations, the Company has retained its rights to develop, manufacture and commercialize ophthalmic products directed to VEGF and Merck has granted the Company a license under certain of its technology solely to develop, manufacture and commercialize RNAi products directed to VEGF.

As of September 30, 2006, the Company has deferred revenue on its balance sheet of \$4.1 million related to upfront cash payments and additional license fee payments received from the Original License Agreement and the Ocular Collaboration Agreement. The Company is recognizing the remaining deferred revenue on a straight-line basis over the period of expected performance or five years. The Company recognized revenues under the Amended License Agreement of \$0.2 million in the three months ended September 30, 2006 and \$0.7 million in the nine months ended September 30, 2006, as compared to \$0.9 million in the three months ended September 30, 2005 and \$3.2 million in the nine months ended September 30, 2005.

***Biogen Idec***

On September 20, 2006, the Company entered into a Collaboration and License Agreement (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 will initially conduct 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. In addition, assuming the successful development and utilization of a product resulting from the collaboration, Biogen Idec will be required to pay Alnylam milestone and royalty payments. The Company did not recognize any revenue for the three months ended September 30, 2006 and has \$5.0 million in deferred revenue on its balance sheet as of September 30, 2006 related to the Biogen Idec Collaboration Agreement.

**Table of Contents**

***Ebola***

On September 28, 2006, the Company was awarded a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus, with the National Institute of Allergy and Infectious Diseases, a component of the National Institutes of Health. The federal contract will provide the Company with up to \$23 million in funding over a four-year period to develop small interfering RNAs ( siRNAs ), the molecules that mediate RNAi, 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 million, the government has committed to pay the Company \$14.2 million over the first two years of the contract and, subject to the progress of the program and budgetary considerations in future years, the remaining \$8.8 million over the last two years of the contract. The Company did not recognize any revenue for the three months ended September 30, 2006 under this Ebola contract.

**4. PUBLIC OFFERING OF COMMON STOCK**

On January 31, 2006, the Company completed a public offering of its common stock. The public offering consisted of the sale and issuance of 5,115,961 shares of the Company s common stock. The price to the public was \$13.00 per share, and proceeds to the Company from the offering, net of expenses, were \$62.2 million. The shares of common stock were registered pursuant to registration statements filed with the SEC in 2006 and 2005.

**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.*

**Overview**

We are a biopharmaceutical company seeking to develop and commercialize new drugs that work through a recently discovered mechanism in cells known as RNA interference, or RNAi. We believe that RNAi therapeutics have the potential to become a major class of drugs with applications in a wide range of therapeutic areas. We have initiated programs to develop RNAi therapeutics that will be administered directly to diseased parts of the body, which we call Direct RNAi therapeutics. We are also working to extend our capabilities by investing in RNAi therapeutics that will be administered systemically in order to treat a broad range of diseases, which we call Systemic RNAi therapeutics. To realize the potential of RNAi therapeutics, we are developing capabilities that we can apply to any specific small interfering RNA, or siRNA, in a systematic way to endow it with drug-like properties. We use the term product platform to describe these capabilities because we believe they will enable us to develop many products across a variety of therapeutic areas. We have not received regulatory approval to market any therapeutics. We initiated human clinical trials of ALN-RSV01, our proprietary RNAi therapeutic for the treatment of patients with respiratory syncytial virus, or RSV, infection in December 2005 and released the results from the trials in May 2006. ALN-RSV01 was found to be safe and well tolerated when administered intranasally in two Phase I clinical studies. In October 2006, we initiated a Phase I study with an inhaled formulation of ALN-RSV01, and we are actively evaluating the initiation of an experimental infection study for later in the year. We plan to initiate a Phase II clinical trial in naturally-infected RSV patients in the first half of 2007.

We commenced operations in June 2002. Since our inception, we have generated significant losses. As of September 30, 2006, we had an accumulated deficit of \$132.1 million. Through September 30, 2006, we have funded our operations primarily through the net proceeds of approximately \$210.3 million from the sale of equity securities, including \$29.9 million in net proceeds from the sale of 5.75 million shares of our common stock from our initial public offering in June 2004, \$58.4 million in net proceeds from the sale of approximately 5.3 million shares of our common stock to Novartis Pharma AG, or Novartis, in October 2005 and approximately \$62.2 million of net proceeds from a follow-on public offering of approximately 5.1 million shares of our common stock in January 2006. Through September 30, 2006, a substantial portion of our total net revenues has been derived from our strategic alliances with Novartis and Merck and Co., Inc., or Merck. For the foreseeable future, we expect our revenues to continue to be derived primarily from strategic alliances, such as our collaborations with Novartis, Merck and Biogen Idec, government contracts and license fee revenues.

We have focused our efforts since inception primarily on business development, research and development, acquiring intellectual property rights, recruiting management and technical staff and raising capital. 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 achieved profitability on a quarterly or annual basis and we expect to incur significant additional losses over the next several years. We expect our net losses to increase primarily due to research and development activities relating to our collaborations, drug development programs and other general



corporate activities. We anticipate that our operating results will fluctuate for the foreseeable future. Therefore, period-to-period comparisons should not be relied upon as predictive of the results in future periods. Our sources of potential funding for the next several years are expected to 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.

**Table of Contents*****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 numerous programs to discover 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 targeted timing for human clinical trials. Our most advanced development program is focused on RSV. In November 2005, we filed an investigational new drug application, or IND, related to our RSV program and initiated human clinical trials of ALN-RSV01 in December 2005. Our second development program is focused on another lung infection, influenza, or flu. In order to optimize delivery and finalize formulation development for ALN-FLU01, the timeline for filing an IND will shift from as early as the end of 2006, to 2007. We also have discovery programs to develop RNAi therapeutics for the treatment of hemorrhagic fever virus, including the Ebola virus; the genetic respiratory disease known as cystic fibrosis, or CF; central nervous system disorders such as spinal cord injury, Parkinson's disease, or PD, Huntington's disease, or HD, neuropathic pain and cardiovascular and metabolic diseases such as hypercholesterolemia; and several other diseases that are the subject of collaborations with Merck, Novartis and Biogen Idec.

A significant component of our business strategy is to enter into strategic alliances and collaborations with pharmaceutical 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 Garching Innovation GmbH, or Garching, 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 two collaborations with Novartis, to discover and develop therapeutics based on RNAi and to develop an RNAi therapeutic for pandemic flu. We have entered into a collaboration agreement with Merck for the development of RNAi technology and therapeutics. In addition, we have entered into an agreement with Cystic Fibrosis Foundation Therapeutics, Inc. to obtain funding and technical resources for our CF program. We also have a collaboration with Medtronic, a leading medical technology company, to focus on developing novel drug-device combinations incorporating RNAi therapeutics for the treatment of neurodegenerative diseases such as PD, HD and Alzheimer's. In September 2006, we entered into a collaboration agreement with Biogen Idec to discover and develop RNAi therapeutics for the potential treatment of progressive multifocal leukoencephalopathy, or PML. In September 2006, we announced that the National Institute of Allergy and Infectious Diseases, or the NIAID, a component of the National Institutes of Health, or the NIH, awarded Alnylam a contract for up to \$23 million over four years to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus. In addition, we have collaborations with the Mayo Foundation for Medical Education and Research and the Mayo Clinic Jacksonville to explore the potential of an RNAi-based treatment for PD, with the University of Texas Southwestern Medical Center at Dallas to explore RNAi therapeutics for the treatment of hypercholesterolemia and with researchers from the University of Georgia and St. Jude Children's Research Hospital to discover and develop an RNAi therapeutic for the treatment and prevention of influenza, as well as other collaborations in connection with our RSV program.

Drug development and approval in the United States is a multi-step process regulated by the U.S. Food and Drug Administration, or FDA. The process begins with the filing of an IND, 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: 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.

The successful development of ALN-RSV01, ALN-FLU01 or any other product candidate we may develop is highly uncertain. There is a risk that any drug discovery and development program may not yield any FDA-approved drugs and/or produce revenue because of the risks inherent in drug discovery and development. Moreover, there are uncertainties specific to any new field of drug discovery, including RNAi. 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 of progress of our pre-clinical trials and other research and development activities;

the scope, rate of progress and cost of our clinical trials of ALN-RSV01 and any other clinical trials we commence in the future;

**Table of Contents**

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 and timing of regulatory approvals;

the cost and timing of establishing sales, marketing and distribution capabilities;

the cost of establishing clinical and commercial supplies of any products that we may develop; and

the effect of competing technological and market developments.

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

**Critical Accounting Policies and Estimates**

There has been one significant change to our critical accounting policies and estimates regarding stock-based compensation since the beginning of this fiscal year. Our other critical accounting policies are described in the *Management Discussion and Analysis of Financial Condition and Results of Operations* section of our Annual Report on Form 10-K for the year ended December 31, 2005.

Effective January 1, 2006, we adopted the fair value recognition provisions of Financial Accounting Standards Board, or FASB, Statement of Financial Accounting Standards, or SFAS, No. 123R, or SFAS 123R, using the modified prospective transition method. Under that transition method, stock-based compensation expense recognized beginning in 2006 includes compensation cost for all stock-based payments granted prior to, but not yet vested as of, January 1, 2006, based on the grant-date fair value estimated in accordance with the original provisions of SFAS No. 123, or SFAS 123, and compensation cost for all stock-based payments granted subsequent to January 1, 2006, based on the grant-date fair value estimated in accordance with the provisions of SFAS 123R. Such amounts are reduced by our estimate of forfeitures of all unvested awards. Results for prior periods have not been restated.

Prior to January 1, 2006, we accounted for employee stock awards granted under our compensation plans in accordance with Accounting Principles Board, or APB, Opinion No. 25, *Accounting for Stock Issued to Employees*, or APB 25, and related interpretations. Under APB 25, when the exercise price of options granted to employees under these plans equals the market price of the common stock on the date of grant, no compensation expense is recorded. When the exercise price of options granted to employees under these plans is less than the market price of the common stock on the date of grant, compensation expense is recognized on a straight-line basis over the vesting period. All stock-based awards granted to non-employees are accounted for at their fair value in accordance with SFAS 123, as amended, and Emerging Issues Task Force, or EITF, Issue No. 96-18, *Accounting for Equity Instruments that are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*, or EITF 96-18, under which compensation expense is generally recognized over the vesting period of the award.

Determining the amount of stock-based compensation to be recorded requires us to develop estimates of fair values of stock options as of the grant date. We calculate the grant date fair values using the Black-Scholes valuation model. Our expected stock price volatility assumption is based on a combination of implied volatilities of similar entities whose share or option prices are publicly available as well as the historical volatility of our publicly traded stock. For stock option grants issued during the three and nine month periods ended September 30, 2006, we used a weighted-average expected stock-price volatility assumption of 67%. Due to our short history of being a public company, we estimated the expected life of option grants made during the three and nine months ended September 30, 2006 using the simplified method prescribed under Staff Accounting Bulletin No. 107 since the grants qualify as plain-vanilla options, which averages the contractual term of the our stock options (10 years) with the vesting term

(2.2 years) for an average of 6.1 years for most stock options. The dividend yield of zero is based on the fact that we have never paid cash dividends and have no present intention to pay cash dividends. The risk-free interest rate used for each grant is based on the U.S. Treasury yield curve in effect at the time of grant for instruments with a similar expected life.

As of September 30, 2006, the estimated fair value of unvested employee awards was \$7.5 million, net of estimated forfeitures. This amount will be recognized over the weighted average remaining vesting period of approximately 1.3 years for these

**Table of Contents**

awards. Stock-based employee compensation was \$1.6 million and \$4.5 million for the three and nine months ended September 30, 2006, respectively. However, the total amount of stock-compensation expense recognized in any future period cannot be predicted at this time because it will depend on levels of stock-based payments granted in the future as well as the portion of the awards that actually vest. SFAS 123R requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. The term forfeitures is distinct from cancellations or expirations and represents only the unvested portion of the surrendered option. We currently expect, based on an analysis of our historical forfeitures, that approximately 84% of our options will actually vest, and therefore have applied an annual forfeiture rate of 4.35% to all unvested options as of September 30, 2006. Ultimately, the actual expense recognized over the vesting period will only be for those shares that vest. Refer to Note 1 Summary of Significant Accounting Policies in our notes to our condensed consolidated financial statements included elsewhere in this Quarterly Report of Form 10-Q for more discussion.

**Results of Operations**

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

	<b>Three Months Ended September 30,</b>		<b>Nine Months Ended September 30,</b>	
	<b>2006</b>	<b>2005</b>	<b>2006</b>	<b>2005</b>
Net revenues	\$ 8,211	\$ 1,413	\$ 19,949	\$ 4,164
Operating expenses	16,815	12,083	49,459	32,719
Loss from operations	\$ (8,604)	\$ (10,670)	\$ (29,510)	\$ (28,555)
Net Loss	\$ (7,400)	\$ (10,678)	\$ (26,170)	\$ (28,423)

**Discussion of Results of Operations for the Three and Nine Months Ended September 30, 2006 and 2005****Revenues**

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

	<b>Three Months Ended September 30,</b>		<b>Nine Months Ended September 30,</b>	
	<b>2006</b>	<b>2005</b>	<b>2006</b>	<b>2005</b>
Revenues from collaboration agreements with Novartis	\$ 6,445	\$	\$ 17,229	\$
Net revenues from collaboration agreements with Merck	216	877	672	3,151
Revenues recorded from InterfeRx program and research reagent licenses	1,230	184	1,415	404
Other revenues	320	352	633	609
Total revenues	\$ 8,211	\$ 1,413	\$ 19,949	\$ 4,164

Under our October 2005 collaboration and license agreement with Novartis, we received an up-front payment totaling \$10.0 million in consideration for rights granted to Novartis under our collaboration and to partly reimburse prior costs incurred by us to develop *in vivo* RNAi technology. In addition, on October 12, 2005, Novartis purchased approximately 5.3 million shares of our common stock at a purchase price of \$11.11 per share for an aggregate purchase price of approximately \$58.5 million. The closing price of our common stock on the date of purchase was \$9.90. We recorded the difference between the purchase price and the closing price of \$6.4 million as deferred revenue. We recognized revenues of \$5.5 million and \$14.3 million under this collaboration with Novartis during the three and nine months ended September 30, 2006, respectively.

Our February 2006 alliance with Novartis for the development of RNAi therapeutics for pandemic flu provides for the reimbursement of research costs incurred under this agreement as well as a share of any future profits. We recognized \$1.0 million and \$2.9 million in revenues during the three and nine months ended September 30, 2006 under the pandemic flu collaboration with Novartis.



**Table of Contents**

In July 2006, we amended our original 2003 collaboration and license agreement with Merck. Also in July 2006, we agreed to terminate our 2004 collaboration and license agreement with Merck for the co-development of RNAi therapeutics for the treatment of ocular diseases. The amended license agreement will focus on the nine targets that remained to be nominated by Merck under the terms of the 2003 license agreement. Three of these nine targets have been nominated by Merck for which we have selected one as a co-development program. These nine programs will be in addition to the existing program directed to the NOGO pathway for which we had already been collaborating with Merck. The initial term of the collaboration under the Amended License Agreement expires in September 2008 and, unless earlier terminated, will continue until the date on which no product is being developed or commercialized under the agreement.

Under our 2003 and 2004 collaboration and license agreements with Merck, we received up-front and license payments, which were deferred and recognized as revenue over the estimated period of performance under these agreements. We recognized revenues of \$0.2 million and \$0.7 million for the three and nine months ended September 30, 2006 as compared to \$0.9 million and \$3.2 million in the three and nine months ended September 30, 2005 under both agreements. The decrease in revenues related to these agreements was due to lower reimbursable AMD program expenses, for which development was suspended in September 2005, based on portfolio management and commercial factors. We have combined the \$4.1 million remaining deferred revenue balance from the September 2003 and June 2004 collaborations and will recognize as revenue on a straight line basis over the remaining estimated life of the collaboration or 5 years.

In addition to our collaboration agreements, we have an InterfeRx program under which we have licensed our intellectual property to others for the development and commercialization of RNAi therapeutics in narrowly defined therapeutic areas in which we are not currently engaged. We have also granted licenses to our intellectual property to others for the development and commercialization of research reagents and services. We expect these programs to provide revenues from license fees and royalties on sales by the licensees, subject to limitations under our agreements with Novartis. We recognized \$1.2 million and \$1.4 million in revenues during the three and nine months ended September 30, 2006 under these programs, as compared to \$0.2 million and \$0.4 million during the three and nine months ended September 30, 2005.

For the foreseeable future, we expect our revenues to continue to be derived primarily from strategic alliances, collaborations and licensing activities.

**Operating expenses**

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

**Three Months Ended September 30, 2006 and 2005**

	Three Months Ended September 30, 2006	% of Total Operating Expenses	Three Months Ended September 30, 2005	% of		Increase (Decrease)
				Total Operating Expenses	Increase (Decrease)	
				\$	%	
Research and development	\$ 12,833	76%	\$ 7,995	66%	\$ 4,838	61%
General and administrative	3,982	24%	4,088	34%	(106)	(3%)
Total operating expenses	\$ 16,815	100%	\$ 12,083	100%	\$ 4,732	39%





**Table of Contents****Nine Months Ended September 30, 2006 and 2005**

	<b>% of</b>		<b>% of</b>		<b>Increase</b>	
	<b>Nine Months</b>	<b>Total</b>	<b>Nine Months</b>	<b>Total</b>	<b>\$</b>	<b>%</b>
	<b>Ended</b>	<b>Operating</b>	<b>Ended</b>	<b>Operating</b>		
	<b>September 30,</b>	<b>Expenses</b>	<b>September 30,</b>	<b>Expenses</b>		
	<b>2006</b>		<b>2005</b>			
Research and development	\$ 37,455	76%	\$ 22,557	69%	\$ 14,898	66%
General and administrative	12,004	24%	10,162	31%	1,842	18%
Total operating expenses	\$ 49,459	100%	\$ 32,719	100%	\$ 16,740	51%

**Research and development**

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

**Three Months Ended September 30, 2006 and 2005**

	<b>% of</b>		<b>% of</b>		<b>Increase (Decrease)</b>	
	<b>Three Months</b>	<b>Expense</b>	<b>Three Months</b>	<b>Expense</b>	<b>\$</b>	<b>%</b>
	<b>Ended</b>	<b>Category</b>	<b>Ended</b>	<b>Category</b>		
	<b>September</b>		<b>September</b>			
	<b>30,</b>		<b>30,</b>			
	<b>2006</b>		<b>2005</b>			
<b>Research and development</b>						
Compensation related	\$ 2,863	22%	\$ 1,888	24%	\$ 975	52%
Non-cash stock-based compensation	883	7%	1,074	13%	(191)	(18%)
External services	1,626	13%	2,071	26%	(445)	(21%)
Clinical trial and manufacturing expenses	1,179	9%		0%	1,179	100%
License fees	2,829	22%	637	8%	2,192	344%
Lab supplies and materials	1,228	9%	842	10%	386	46%
Facilities-related expenses	1,623	13%	1,106	14%	517	47%
Other	602	5%	377	5%	225	60%
<b>Total research and development</b>	\$ 12,833	100%	\$ 7,995	100%	\$ 4,838	61%

As indicated in the table above, the increase in research and development expenses in the three months ended September 30, 2006 as compared to the three months ended September 30, 2005 was primarily due to license fees, which consist of \$1.9 million in fees related to our collaboration with Inex focused on the systemic delivery of RNAi therapeutics and \$0.8 million in fees with Isis in connection with our Biogen Idec collaboration during the three

months ended September 30, 2006. In addition, we had increased clinical trial and manufacturing related expenses in support of our RSV clinical program, which began in December 2005. The increase in compensation related expenses, facilities-related expenses and lab supplies and materials expenses was due to additional research and development headcount over the past year to support our alliances and expanding product pipeline. We expect to continue to devote a substantial portion of our resources to research and development expenses and that research and development expenses will increase as we continue development of our and our collaborators' product candidates and technologies.

**Table of Contents****Nine Months Ended September 30, 2006 and 2005**

	<b>Nine Months Ended September 30, 2006</b>	<b>% of Expense Category</b>	<b>Nine Months Ended September 30, 2005</b>	<b>% of Expense Category</b>	<b>Increase (Decrease) \$ %</b>	
<b>Research and development</b>						
Compensation related	\$ 7,743	21%	\$ 5,087	23%	\$ 2,656	52%
Non-cash stock-based compensation	3,331	9%	1,815	8%	1,516	84%
External services	4,451	12%	5,615	25%	(1,164)	(21%)
Clinical trial and manufacturing expenses	7,618	20%		0%	7,618	100%
License fees	3,955	11%	2,906	13%	1,049	36%
Lab supplies and materials	4,174	11%	2,769	12%	1,405	51%
Facilities-related expenses	4,506	12%	3,341	15%	1,165	35%
Other	1,677	4%	1,024	4%	653	64%
<b>Total research and development</b>	<b>\$ 37,455</b>	<b>100%</b>	<b>\$ 22,557</b>	<b>100%</b>	<b>\$ 14,898</b>	<b>66%</b>

As indicated in the table above, the increase in research and development expenses in the nine months ended September 30, 2006 as compared to the nine months ended September 30, 2005 was primarily due to clinical trial and manufacturing related expenses in support of our RSV clinical program, which began in December 2005. The increase in compensation related expenses and lab supplies and materials expenses was due to additional research and development headcount over the past year to support our alliances and expanding product pipeline. The increase in stock-based compensation for the nine months ended September 30, 2006 was primarily due to our adoption of SFAS 123R on January 1, 2006. 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.

Prior to July 1, 2004, we did not track any of our research and development costs or our personnel and personnel-related costs on a project-by-project basis, because the majority of our efforts were focused on the development of capabilities associated with our product platform rather than on specific projects. In July 2004, we began work under our agreement with Merck for the co-development of RNAi ocular therapeutics, or the Ocular Agreement. In July 2006, we terminated the Ocular Agreement and entered into an amended and restated research collaboration and license agreement with Merck, which we refer to as the Amended Collaboration Agreement. Both the Ocular Agreement and the Amended Collaboration Agreement contain a cost sharing arrangement whereby each party reimburses the other for 50% of the costs incurred under the project, as defined by the agreement. Costs reimbursed under the agreements include certain direct external costs and a negotiated full-time equivalent labor rate for the actual time worked on the project. As a result, in July 2004, we began tracking direct external costs attributable to, and the actual time our employees worked on, the Ocular Agreement, and continue to do so for purposes of the Amended Collaboration Agreement. However, a significant portion of our research and development expenses are not tracked on a project-by-project basis. In addition, as of September 30, 2006, the majority of our research programs were in the preclinical phase, meaning that we were conducting formulation, efficacy, pharmacology and/or toxicology testing of compounds in animal models and/or biochemical assays. We initiated our first human clinical trials for our proprietary RNAi therapeutic for the treatment of patients with RSV during the fourth quarter of 2005.

***General and administrative***

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

**Table of Contents****Three Months Ended September 30, 2006 and 2005**

	<b>Three Months Ended September 30, 2006</b>	<b>% of Expense Category</b>	<b>Three Months Ended September 30, 2005</b>	<b>% of Expense Category</b>	<b>Increase (Decrease) \$ %</b>	
<b>General and administrative</b>						
Compensation related	\$ 921	23%	\$ 847	21%	\$ 74	9%
Consulting and professional services	937	24%	1,231	30%	(294)	(24%)
Facilities related	751	19%	436	11%	315	72%
Non-cash stock-based compensation	831	21%	1,122	27%	(291)	(26%)
Insurance	171	4%	153	4%	18	12%
Other	371	9%	299	7%	72	24%
<b>Total general and administrative</b>	<b>\$ 3,982</b>	<b>100%</b>	<b>\$ 4,088</b>	<b>100%</b>	<b>(\$106)</b>	<b>(3%)</b>

As indicated in the table above, the slight decrease in general and administrative expenses during the three months ended September 30, 2006 as compared to the three months ended September 30, 2005 was primarily due to lower non-cash stock-based compensation expenses as a result of the vesting of a common stock option upon the closing of the transactions with Novartis during the three months ended September 30, 2005, as well as lower legal and professional service fees, which were higher during the three months ended September 30, 2005 because of increased business activities associated with entering into the Novartis Collaboration during the third quarter of 2005 offset by higher facilities related costs due to the expansion of our facilities during 2006.

**Nine Months Ended September 30, 2006 and 2005**

	<b>Nine Months Ended September 30, 2006</b>	<b>% of Expense Category</b>	<b>Nine Months Ended September 30, 2005</b>	<b>% of Expense Category</b>	<b>Increase \$ %</b>	
<b>General and administrative</b>						
Compensation related	\$ 2,609	22%	\$ 2,478	24%	\$ 131	5%
Consulting and professional services	3,281	27%	2,950	29%	331	11%
Facilities related	2,009	17%	1,420	14%	589	41%
Non-cash stock-based compensation	2,364	20%	1,780	18%	584	33%
Insurance	488	4%	459	5%	29	6%
Other	1,253	10%	1,075	10%	178	17%
	<b>\$ 12,004</b>	<b>100%</b>	<b>\$ 10,162</b>	<b>100%</b>	<b>\$ 1,842</b>	<b>18%</b>

**Total general and administrative**

As indicated in the table above, the increase in general and administrative expenses during the nine months ended September 30, 2006 as compared to the nine months ended September 30, 2005 was primarily due to higher stock-based compensation expenses related to our adoption of SFAS No. 123R on January 1, 2006, higher facilities related costs due to the expansion of our facilities during 2006 as well as higher legal and professional service fees due to increased business activities during the nine months ended September 30, 2006.

***Interest income, interest expense and other***

Interest income was \$1.6 million for the three months ended September 30, 2006 and \$4.4 million for the nine months ended September 30, 2006 compared to \$0.2 million for the three months ended September 30, 2005 and \$0.8 million for the nine months ended September 30, 2005. The increase was due to our higher average cash, cash equivalent and marketable securities balances due primarily from our January 2006 public offering of common stock and higher average interest rates during the three and nine months ended September 30, 2006.

**Table of Contents**

Interest expense was \$0.3 million for the three months ended September 30, 2006 and \$0.7 million for the nine months ended September 30, 2006 compared to \$0.2 million for the three months ended September 30, 2005 and \$0.7 million for the nine months ended September 30, 2005. The slight increase was due to higher amounts of outstanding debt during the three and nine months ended September 30, 2006.

**Liquidity and Capital Resources**

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

	<b>Nine Months Ended September</b>	
	<b>30,</b>	
	<b>2006</b>	<b>2005</b>
Net loss	\$ (26,170)	\$ (28,423)
Adjustments to reconcile net loss to net cash used in operating activities	8,784	7,965
Changes in operating assets and liabilities	(2,631)	357
Net cash used in operating activities	(20,017)	(20,101)
Net cash (used in) provided by investing activities	(25,207)	6,796
Net cash provided by financing activities	64,935	466
Effect of exchange rate on cash	48	(255)
Net increase (decrease) in cash and cash equivalents	19,759	(13,094)
Cash and cash equivalents, beginning of period	15,757	20,272
Cash and cash equivalents, end of period	\$ 35,516	\$ 7,178

We commenced operations in June 2002 and, since our inception, we have generated significant losses. As of September 30, 2006, we had an accumulated deficit of \$132.1 million. As of September 30, 2006, we had cash, cash equivalents and marketable securities of \$120.3 million, compared to cash, cash equivalents and marketable securities of \$80.0 million as of December 31, 2005. 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 nine months ended September 30, 2006 as our use of cash in our operating activities remained relatively consistent as compared to the nine months ended September 30, 2005. The main components of our use of cash in operating activities are the net loss and changes in our operating assets and liabilities. 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 stock-based compensation, depreciation and amortization. Non-cash stock-based compensation increased due primarily to our adoption of SFAS 123R on January 1, 2006 as well as to a lesser extent the increase of the fair value of non-employee stock options. In addition, we received \$1.1 million in proceeds from our landlord for tenant improvements at our Cambridge facility. We also had an increase in accrued expenses of \$1.3 million for the nine months ended September 30, 2006. These increases were offset by a net accounts receivable increase of \$4.2 million and amortization of deferred revenue of \$1.4 million for the nine months ended September 30, 2006. Our cash utilization is expected to continue for the remainder of 2006 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 nine months ended September 30, 2006, net cash used in investing activities of approximately \$25.2 million resulted from net purchases of marketable securities of approximately \$20.5 million as well as purchases of property and equipment of approximately \$4.7 million. For the nine months ended September 30, 2005, net cash provided by investing activities resulted from net sales of marketable securities of approximately \$8.1 million, partially offset by purchases of property and equipment of approximately \$1.3 million.

**Table of Contents*****Financing activities***

For the nine months ended September 30, 2006, our financing activities provided \$64.9 million, reflecting the net proceeds of \$62.2 million from our follow-on public offering in January 2006 as well as proceeds of \$0.6 million from stock option exercises. In addition, we borrowed \$3.6 million under our line of credit with Oxford Finance Corporation, or Oxford, offset by debt payments of \$1.5 million.

In March 2006, we entered into an agreement with Oxford to establish an equipment line of credit for up to \$7.0 million, available through June 2007, and we borrowed an aggregate of approximately \$388,000 from Oxford pursuant to the security agreement. Of such amount, approximately \$241,000 bears interest at a fixed rate of 10.07% and is required to be repaid in 48 monthly installments of principal and interest beginning in March 2006. The remainder of such amount, approximately \$147,000, bears interest at a fixed rate of 10.09% and is required to be repaid in 36 monthly installments of principal and interest beginning in March 2006. In June 2006, we borrowed approximately \$2.3 million pursuant to the agreement. Of such amount, approximately \$2.1 million bears interest at a fixed rate of 10.37% and is required to be repaid in 36 monthly installments of principal and interest beginning in June 2006. The remainder of such amount, approximately \$0.2 million, bears interest at a fixed rate of 10.35% and is required to be repaid in 48 monthly installments of principal and interest beginning in June 2006.

In March 2004, we entered into an agreement with Lighthouse Capital Partners V, L.P. to establish an equipment line of credit for \$10.0 million. In June 2005, the parties amended the agreement to allow us the ability to draw down amounts under the line of credit through December 31, 2005 upon adherence to certain conditions. All borrowings under the line of credit are collateralized by the assets financed and the agreement contains certain provisions that restrict our ability to dispose of or transfer these assets. As of June 30, 2006, there was \$6.5 million outstanding under this line of credit, \$6.2 million of which bears interest at a fixed rate of 9.25% and \$0.3 million of 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 drawdowns made during the period from March 26, 2004 through June 30, 2005 at which point all drawdowns began to be repaid over 48 months. On the maturity of each equipment advance under the line of credit, we are required to pay, in addition to the 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 September 30, 2006, we had an aggregate outstanding balance of \$9.5 million under all our loan agreements.

Based on our current operating plan, we believe that our existing resources, together with the cash we expect to generate under our current alliances, will be sufficient to fund our planned operations beyond the end of 2007, during which time we expect to extend the capabilities of our technology platform, further the development of our products, conduct clinical trials and continue to prosecute patent applications and otherwise build and maintain our patent portfolio. However, we may require significant additional funds earlier than we currently expect in order to develop, and commence clinical trials for, any product candidates.

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;

## **Table of Contents**

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.

### **Off-Balance Sheet Arrangements**

We do not have any off-balance sheet arrangements or relationships with unconsolidated entities or financial partnerships, such as entities often referred to as structured finance or special purpose entities.

### **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, 2005. In addition, in June 2006, we borrowed approximately \$2.3 million pursuant to our line of credit with Oxford. Of such amount, approximately \$2.1 million bears interest at a fixed rate of 10.37% and is required to be repaid in 36 monthly installments of principal and interest beginning in June 2006. The remainder of such amount, approximately \$0.2 million, bears interest at a fixed rate of 10.35% and is required to be repaid in 48 monthly installments of principal and interest beginning in June 2006. In August 2006, we borrowed approximately \$1.1 million pursuant to our line of credit with Oxford. Of such amount, approximately \$0.6 million bears interest at a fixed rate of 10.39% and is required to be repaid in 48 monthly installments of principal and interest beginning in August 2006. The remainder of such amount, approximately \$0.5 million, bears interest at a fixed rate of 10.41% and is required to be repaid in 36 equal monthly installments of principal and interest beginning in August 2006. Other than this additional debt, there have been no material changes in our contractual obligations and commitments since December 31, 2005.

### **Recently Issued Accounting Pronouncements**

In July 2006, the FASB issued FASB Interpretation No. 48, Accounting for Uncertainty in Income Taxes, or FIN 48, which clarifies the accounting for uncertainty in income taxes recognized in a company's financial statements in accordance with FASB Statement No. 109, Accounting for Income Taxes. FIN 48 prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. This interpretation also provides guidance on derecognition, classification, interest and penalties, accounting in interim periods, disclosure, and transition. FIN 48 is effective for fiscal years beginning after December 15, 2006. We are currently assessing the impact, if any, of FIN 48 on our financial position and results of operations.

In September 2006, the FASB issued 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 currently evaluating the impact of SFAS No. 157 on our financial statements.

In September 2006, the U.S. Securities and Exchange Commission staff issued Staff Accounting Bulletin No. 108, or SAB 108, Considering the Effects of Prior Year Misstatements when Quantifying Misstatements in Current Year Financial Statements. SAB 108 eliminates the diversity of practice surrounding how public companies quantify financial statement misstatements. It establishes an approach that requires quantification of financial statement misstatements based on the effects of the misstatements on each of the company's financial statements and the related

financial statement disclosures. SAB 108 must be applied to annual financial statements for their first fiscal year ending after November 15, 2006. We do not expect SAB 108 to have a material impact on our financial condition or results of operations.

**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 would impact the net fair value of such interest-sensitive financial instruments by less than \$200,000.

*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 periodic funding to support these operations. The amount of this funding is based upon actual expenditures incurred by our European operations and is calculated in Euros. Because of the frequency with which these operations are funded, we record amounts payable to fund these operations as current liabilities, which eliminate upon consolidation. 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 condensed 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 2005 and the timing of the funding of these operations were to remain consistent during the remainder of 2006, a constant increase or decrease in the exchange rate between the Euro and the United States Dollar during the remainder of 2006 of 10% would result in a foreign exchange gain or loss of approximately \$50,000.

The amount of our foreign currency exchange rate risk is based on many factors including the timing and size of fluctuations in the currency exchange rate between the Euro and the United States Dollar, the amount of actual expenditures incurred by our European operations and the timing and size of funding provided to our European operations from the United States.

**ITEM 4. CONTROLS AND PROCEDURES**

Our management, with the participation of our chief executive officer and vice president of finance and treasurer, evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2006. 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 submit under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of September 30, 2006, 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 fiscal quarter ended September 30, 2006 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**

*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 RNA interference, or 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 September 30, 2006, we had an accumulated deficit of \$132.1 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 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. If we are unable to secure revenue from collaborations, we may be unable to continue our efforts to discover, develop and commercialize RNAi therapeutics without raising financing from other sources.

To become and remain 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 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;

**Table of Contents**

our ability to establish and maintain additional collaborative arrangements;

the resources, time and costs required to initiate and complete our pre-clinical and clinical trials, obtain regulatory approvals, protect our intellectual property and obtain and maintain licenses to third-party intellectual property; 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 Pharma AG, or Novartis, provides Novartis with the right generally to maintain its ownership percentage in Alnylam. 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 and either party may terminate this collaboration in the event of a material uncured breach by the other party. 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.

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

Our current collaborations allow, and we expect that any future collaborations will allow, either party to terminate the collaboration for a material breach by the other party. If a collaborator terminates its collaboration with us, for breach or otherwise, it would be difficult for us to attract new collaborators and could adversely affect how we are perceived in the business and financial communities. In addition, a collaborator 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.

**Table of Contents**

***We depend on a government contract 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 National Institute of Allergy and Infectious Diseases, or the NIAID, a component of the National Institutes of Health, or the NIH, awarded us a contract for up to \$23 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 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 million we expect to receive under this contract, we may not be able to develop therapeutics to treat Ebola.

***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 of 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 have contracted with Dowpharma contract manufacturing services, a business unit of The Dow Chemical Company, for supply of material to meet our testing needs for toxicology and clinical testing. There are risks inherent in pharmaceutical manufacturing that could affect Dowpharma's ability to meet our delivery time requirements or provide adequate amounts of material to meet our needs. Included in these risks are synthesis and/or purification failures and contamination during the manufacturing process, both of which could result in unusable product and cause delays in our development process. The manufacturing process for any products that we may develop is an element of the U.S. Food and Drug Administration, or FDA, approval process and we will need to contract with manufacturers who can meet the 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. 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



## **Table of Contents**

party manufacture our products.

***We have no sales, marketing or distribution experience and expect to depend significantly on third parties who may not successfully commercialize our products.***

We have no sales, marketing or distribution experience. We expect to rely heavily on third parties to launch and market certain of our product candidates, if approved. We may have limited or no control over the sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties.

To develop internal sales, distribution and marketing capabilities, we will have to invest significant amounts of financial and management resources. For products where we decide to perform sales, marketing and distribution functions ourselves, we could face a number of additional risks, including:

we may not be able to attract and build a significant marketing or sales force;

the cost of establishing a marketing or sales force may not be justifiable in light of the revenues generated by any particular product; and

our direct sales and marketing efforts may not be successful.

### **Risks Related to Managing Our Operations**

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

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

Although we have generally been successful in our recruiting efforts, we face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions. We may be unable to attract and retain suitably qualified individuals, and our failure to do so could have an adverse effect on our ability to implement our business plan.

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

Since we commenced operations in 2002, we have grown to over 110 full time equivalent employees, with offices and laboratory space in both Cambridge, Massachusetts and Kulmbach, Germany. This rapid and substantial growth, and the geographical separation of our sites, has placed a strain on our administrative and operational infrastructure, and we anticipate that our continued growth will have a similar impact. 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.

***If we are unable to manage the challenges associated with our international operations, the growth of our business could be limited.***

In addition to our operations in Cambridge, Massachusetts, we operate an office and laboratory in Kulmbach, Germany. We are subject to a number of risks and challenges that specifically relate to these international operations. Our international operations may not be successful if we are unable to meet and overcome these challenges, which could limit the growth of our business and may have an adverse effect on our business and operating results. These risks include:



**Table of Contents**

fluctuations in foreign currency exchange rates that may increase the U.S. dollar cost of our international operations;

difficulty managing operations in multiple locations, which could adversely affect the progress of our product candidate development program and business prospects;

local regulations that may restrict or impair our ability to conduct biotechnology-based research and development;

**Table of Contents**

foreign protectionist laws and business practices that favor local competition; and

failure of local laws to provide the same degree of protection against infringement of our intellectual property, which could adversely affect our ability to develop product candidates or reduce future product or royalty revenues, if any, from product candidates we may develop.

**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 have one product candidate, ALN-RSV01, being developed for the treatment of respiratory syncytial virus, or RSV, infection for which we recently completed two Phase I clinical trials and for which another Phase I clinical trial recently began during October 2006. We may not be able to further advance any product candidates into clinical trials. Even if we do 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 human clinical trials. We, the FDA or other applicable regulatory authorities may suspend clinical trials of a drug candidate at any time if we or they believe the subjects or patients participating in such trials are being exposed to unacceptable health risks, or for other reasons. 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 nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease 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 institutional review boards, referred to as 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 or suspend 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;

discussions with 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 IRB approval of studies;

delays in enrolling patients and volunteers into clinical trials;

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

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



**Table of Contents**

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 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. 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 delivery of Direct 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 Direct RNAi therapeutics, which could negatively affect our ability to successfully commercialize certain Direct RNAi therapeutics.

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

Our drug candidates are subject to extensive governmental regulations relating to development, clinical trials, manufacturing and commercialization. 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 sold. 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 little 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 exceeds five 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 we expect any product candidates that we develop will be 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 are approved treatments for RSV and PD, 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

## **Table of Contents**

indicated uses for which we may market the product. These limitations may limit the size of the market for the product.

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.

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

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

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

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

regulators or IRBs 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

the 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 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 FDA review.

## **Table of Contents**

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 prosecutions.

***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 products.

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;

the willingness of patients to accept relatively new routes of administration;

the success of our physician education programs;

the availability of government and third-party payor reimbursement;

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

the availability of alternative effective treatments for the diseases that product candidates we develop are intended to treat.

***Even if we develop RNAi therapeutic products for the prevention or treatment of infection by pandemic flu virus and/or Ebola, governments may not elect to purchase such products, which could adversely affect our business.***

We expect that governments will be the only purchasers of any products we may develop for the prevention or treatment of pandemic flu virus or 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 virus 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 under development successfully and could harm our reputation and lead to reduced acceptance of our products by the market. These enforcement actions include:

warning letters;

recalls or public notification or medical product safety alerts;

restrictions on, or prohibitions against, marketing our products;

restrictions on importation of our products;

35

---

**Table of Contents**

suspension of review or refusal to approve pending applications;

suspension or withdrawal of product approvals;

product seizures;

injunctions; and

civil and criminal penalties and fines.

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

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

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

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

they are incident to a physician's services;

they are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standard of medical practice;

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,

**Table of Contents**

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, requires 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 retains the discretion not to implement a drug reimportation plan if he finds that the benefits do not outweigh the cost. Proponents of drug reimportation may attempt to pass legislation that would directly allow reimportation under certain circumstances. If legislation or regulations were passed allowing the reimportation of drugs, they 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. So far, these programs have not led to a large proportion of prescription orders to be placed for foreign purchase. The FDA has warned that importing drugs is illegal and in December 2004 began to take action to halt the use of these programs by filing a civil complaint against an importer of foreign prescription drugs. If such programs were to become more substantial and were not to be encumbered by the federal government, they could also decrease the price we receive for any products that we may develop, 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, or limitations on the indications for which they may be used, or suspension or withdrawal of approval. 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 Germany that are required for our research and development activities. 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 employ 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.

**Table of Contents**

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 any drugs that we develop.*

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

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

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

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

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

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

We will face intense competition from drugs that have already been approved and accepted by the medical community for the treatment of the conditions for which we may develop drugs. We also expect to face competition from new drugs that enter the market. We believe a significant number of drugs are currently under development, and may become commercially available in the future, for the treatment of conditions for which we may try to develop drugs. For instance, we are currently evaluating RNAi therapeutics for RSV, flu, Ebola, PD, hypercholesterolemia, neuropathic pain, PML and CF. Virazole is currently marketed for the treatment of certain RSV patients, Tamiflu(R) and Relenza(R) are marketed for the treatment of flu patients, numerous drugs are currently marketed for the treatment of hypercholesterolemia, PD and neuropathic pain and two drugs, TOBI(R) and Pulmozyme(R), are currently marketed for the treatment of CF. These drugs, or other of our competitors' products, may be more effective, 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.

**Table of Contents**

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, including Sirna Therapeutics, Inc., which recently announced that it was being acquired by Merck, Natestch Pharmaceuticals, Inc., Acuity Pharmaceuticals, Inc., Nucleonics, Inc., SR Pharma and CytRx Corporation. In addition, we granted licenses to Isis, GeneCare, Benitec, Natestch, Calando Pharmaceuticals, 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, therefore, a licensee under our intellectual property for specified disease targets. However, if Merck's proposed acquisition of Sirna is completed, Merck, which has substantially more resources than we do, could become a direct competitor.

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 multiple antisense drug candidates 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 mere 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 or circumvented. Moreover, the United

States Patent and Trademark Office, or USPTO may commence interference proceedings involving our patents or patent applications. Any challenge to, 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

**Table of Contents**

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 Pharmaceuticals, Inc., Inex, Idera Pharmaceuticals, Inc., Carnegie Institution of Washington, Cancer Research Technology Limited, the Massachusetts Institute of Technology, the Whitehead Institute, Garching Innovation GmbH, representing the Max Planck Gesellschaft zur Förderung der Wissenschaften e.V., referred to as the Max Planck organization, Stanford University, Cold Spring Harbor Laboratory and the University of South Alabama. We also intend to enter into additional licenses to third party intellectual property in the future.

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

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

RNA interference is a relatively new scientific field that has generated many different patent applications from organizations and individuals seeking to obtain important patents in the field. 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 may, however, be appealed. If appealed, 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 the 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. 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

**Table of Contents**

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

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

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

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

For two important patents, owned in part or solely by the Max Planck organization of Germany, our amended licenses with Garching Innovation GmbH, a related entity to the Max Planck organization, require us to maintain a minimum level of employees in Germany. If we fail to comply with this condition, the owners of the patents that are the subject of these licenses may have the right to grant a similar license to one other company. We regard these patents as significant because they relate to important aspects of the structure of siRNA molecules and their use as therapeutics.

We have an agreement with Isis under which we were granted licenses to over 150 patents and patent applications that we believe will be useful to the development of RNAi therapeutics. If, by January 1, 2008, we or a collaborator have not completed the studies required for an investigational new drug application filing or similar foreign filing for at least one product candidate involving these patent rights, Isis would have the right to grant licenses to third parties

for these patents and patent applications, thereby making our rights non-exclusive.

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

**Table of Contents**

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

**Risks Related to Our Common Stock*****If our stock price fluctuates, purchasers of our common stock could incur substantial losses.***

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

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

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

***If there are substantial sales of our common stock, the price of our common stock could decline.***

Substantially all of the outstanding shares of our common stock are freely tradable, tradable under Rule 144 or held by holders with demand registration rights.

As of September 30, 2006, the holders of approximately 6.8 million shares of our common stock have rights to require us to file registration statements under the Securities Act of 1933, as amended, or the Securities Act, or to include their shares in registration statements that we may file in the future for ourselves or other stockholders. If our existing stockholders sell a large number of shares of our common stock or the public market perceives that existing stockholders might sell shares of common stock, the market price of our common stock could decline significantly.

***Novartis ownership of our common stock could delay or prevent a change in corporate control.***

Novartis holds approximately 16% of our outstanding common stock as of September 30, 2006. 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 shareholder 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



**Table of Contents**

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.

**Table of Contents**

In addition, in July 2005, our board of directors adopted a shareholder rights plan, the provisions of which could make it more 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 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS**

In July 2006, we issued an aggregate of 8,594 shares of our common stock pursuant to and in accordance with the terms of the Co-Exclusive License Agreement, dated December 20, 2002, as amended, by and among us, Garching Innovation GmbH, or Garching, and Alnylam U.S., Inc., our wholly-owned subsidiary. Under the license agreement, we were required to issue these shares, as instructed by Garching, upon the issuance of Patent No. 7,056,704. Pursuant to Garching's instructions, we issued the shares to Max Planck Gesellschaft zur Foerderung de Wissenschaften e.V., or MaxPlanck, Whitehead Institute for Biomedical Research, or WI, Massachusetts Institute of Technology, or MIT, European Molecular Biology Laboratory, or EMBL, and EMBL Enterprise Management Technology Transfer GmbH, or EMBLEM.

The shares of common stock issued to MaxPlanck, EMBL and EMBLEM were issued in reliance on exemptions from the registration provisions of the Securities Act set forth in Regulation S promulgated thereunder relative to sales by an issuer outside of the United States. In connection with these issuances, each of MaxPlanck, EMBL and EMBLEM represented to us that it is not a U.S. person and was not acquiring the shares for the account or benefit of any U.S. person and agreed that it will resell such shares only in accordance with the provisions of Regulation S and will not engage in any hedging transactions involving the shares of common stock in violation of the Securities Act.

The shares of common stock issued to WI and MIT were issued in reliance on exemptions from the registration provisions of the Securities Act, set forth in Section 4(2) thereunder relative to sales by an issuer not involving a public offering. In connection with these issuances, each of WI and MIT represented to us that it is an accredited investor, is acquiring the shares for investment and not distribution, can bear the risks of the investment and can hold the shares for an indefinite period of time.

**ITEM 6. EXHIBITS**

- 10.1 Collaboration and License Agreement by and between the Registrant and Biogen Iden MA, Inc. dated September 20, 2006.
- 10.2 Letter Agreement by and between the Registrant and Vincent J. Miles effective as of October 20, 2006.
- 31.1 Certification of President and Chief Executive Officer of Alnylam Pharmaceuticals, Inc. pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
- 31.2 Certification of Vice President of Finance and Treasurer of Alnylam Pharmaceuticals, Inc. pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
- 32.1 Certification of President and Chief Executive Officer of Alnylam Pharmaceuticals, Inc. 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 Vice President of Finance and Treasurer of Alnylam Pharmaceuticals, Inc. 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**

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

45

---

**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: November 9, 2006

By: /s/ John M. Maraganore

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

Date: November 9, 2006

By: /s/ Patricia L. Allen

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

46