ALNYLAM PHARMACEUTICALS, INC.
Form 10-Q
August 03, 2011

Table of Contents

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

FORM 10-Q

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

For the quarterly period ended June 30, 2011

OR

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

For the transition period from _____ to _____

Commission File Number 000-50743

ALNYLAM PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware	77-0602661
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
300 Third Street, Cambridge, MA	02142
(Address of Principal Executive Offices)	(Zip Code)

(617) 551-8200

(Registrant s Telephone Number, Including Area Code)

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes þ No o

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

Large accelerated filer o	Accelerated filer þ	Non-accelerated filer o	Smaller reporting company o

(do not check if smaller reporting company)

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

At July 29, 2011, the registrant had 42,651,782 shares of Common Stock, $0.01 par value per share, outstanding.

INDEX

	PAGE NUMBER
PART I. FINANCIAL INFORMATION	
ITEM 1. FINANCIAL STATEMENTS (Unaudited)	
CONDENSED CONSOLIDATED BALANCE SHEETS AS OF JUNE 30, 2011 AND DECEMBER 31, 2010	2
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS FOR THE THREE AND SIX MONTHS ENDED JUNE 30, 2011 AND 2010	3
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS FOR THE SIX MONTHS ENDED JUNE 30, 2011 AND 2010	4
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS	5
ITEM 2. MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS	16
ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK	28
ITEM 4. CONTROLS AND PROCEDURES	28
PART II. OTHER INFORMATION	
ITEM 1. LEGAL PROCEEDINGS	29
ITEM 1A. RISK FACTORS	30
ITEM 5. OTHER INFORMATION	52
ITEM 6. EXHIBITS	53
SIGNATURES	54

EX-12
EX-31.1
EX-31.2
EX-32.1
EX-32.2
EX-101 INSTANCE DOCUMENT
EX-101 SCHEMA DOCUMENT
EX-101 CALCULATION LINKBASE DOCUMENT
EX-101 LABELS LINKBASE DOCUMENT
EX-101 PRESENTATION LINKBASE DOCUMENT

Table of Contents

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

	June 30, 2011	December 31, 2010
ASSETS		
Current assets:		
Cash and cash equivalents	$ 67,110	$ 74,599
Marketable securities	150,839	158,532
Collaboration receivables	1,308	3,450
Income taxes receivable		10,669
Prepaid expenses and other current assets	5,077	6,889
Total current assets	224,334	254,139
Marketable securities	98,080	116,773
Property and equipment, net	16,252	18,289
Investment in joint venture (Regulus Therapeutics Inc.)	1,801	3,616
Intangible assets, net	361	448
Total assets	$ 340,828	$ 393,265
LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	$ 7,949	$ 9,312
Accrued expenses	11,380	11,116
Deferred rent	484	484
Deferred revenue	80,721	81,134
Total current liabilities	100,534	102,046
Deferred rent, net of current portion	2,879	2,869
Deferred revenue, net of current portion	100,122	129,974
Other long-term liabilities	742	143
Total liabilities	204,277	235,032
Commitments and contingencies (Notes 4, 5 and 6)		
Stockholders equity:		
Preferred stock, $0.01 par value, 5,000,000 shares authorized and no shares issued and outstanding at June 30, 2011 and December 31, 2010		
Common stock, $0.01 par value, 125,000,000 shares authorized; 42,653,915 shares issued and outstanding at June 30, 2011; 42,343,423 shares issued and outstanding at December 31, 2010	427	423
Additional paid-in capital	509,826	500,443
Accumulated other comprehensive (loss) income	(246)	714
Accumulated deficit	(373,456)	(343,347)

Total stockholders equity	136,551	158,233
Total liabilities and stockholders equity	$ 340,828	$ 393,265

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

Table of Contents

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2011	2010	2011	2010
Net revenues from research collaborators	$ 20,614	$ 26,617	$ 41,511	$ 51,181
Operating expenses:				
Research and development [1]	25,303	28,136	51,652	52,836
General and administrative [1]	8,429	10,107	18,653	21,277
Total operating expenses	33,732	38,243	70,305	74,113
Loss from operations	(13,118)	(11,626)	(28,794)	(22,932)
Other income (expense):				
Equity in loss of joint venture (Regulus Therapeutics Inc.)	(1,012)	(3,919)	(2,084)	(5,497)
Interest income	322	641	704	1,231
Other (expense) income	(16)	43	65	32
Total other income (expense)	(706)	(3,235)	(1,315)	(4,234)
Loss before income taxes	(13,824)	(14,861)	(30,109)	(27,166)
Benefit from income taxes		229		211
Net loss	$ (13,824)	$ (14,632)	$ (30,109)	$ (26,955)
Net loss per common share basic and diluted	$ (0.33)	$ (0.35)	$ (0.71)	$ (0.64)
Weighted average common shares used to compute basic and diluted net loss per common share	42,379	41,991	42,369	41,920
Comprehensive loss:				
Net loss	$ (13,824)	$ (14,632)	$ (30,109)	$ (26,955)
Foreign currency translation		(29)		(29)
Unrealized (loss) gain on marketable securities	(228)	492	(960)	599
Comprehensive loss	$ (14,052)	$ (14,169)	$ (31,069)	$ (26,385)

(1) Non-cash stock-based compensation expenses included in operating expenses are as follows:				
Research and development	$ 2,830	$ 3,246	$ 5,495	$ 6,475
General and administrative	1,384	1,822	2,841	3,920

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

Table of Contents

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

	Six Months Ended June 30,	
	2011	**2010**
Cash flows from operating activities:		
Net loss	$ (30,109)	$ (26,955)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Depreciation and amortization	2,626	2,384
Deferred income taxes		(144)
Non-cash income tax benefit		(216)
Non-cash stock-based compensation	8,336	10,395
Charge for 401(k) company stock match	274	271
Equity in loss of joint venture (Regulus Therapeutics Inc.)	2,084	5,497
Changes in operating assets and liabilities:		
Collaboration receivables	2,142	(314)
Income taxes receivable	10,669	
Prepaid expenses and other assets	1,812	(1,870)
Accounts payable	(1,363)	(2,091)
Income taxes payable		(5,547)
Accrued expenses and other	910	(2,570)
Deferred revenue	(30,265)	(18,755)
Net cash used in operating activities	(32,884)	(39,915)
Cash flows from investing activities:		
Purchases of property and equipment	(502)	(2,527)
Purchases of marketable securities	(163,759)	(182,076)
Sales and maturities of marketable securities	189,185	150,178
Net cash provided by (used in) investing activities	24,924	(34,425)
Cash flows from financing activities:		
Proceeds from issuance of common stock	471	2,090
Proceeds from issuance of shares to Novartis		993
Net cash provided by financing activities	471	3,083
Effect of exchange rate on cash		(29)
Net decrease in cash and cash equivalents	(7,489)	(71,286)
Cash and cash equivalents, beginning of period	74,599	137,468
Cash and cash equivalents, end of period	$ 67,110	$ 66,182

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

Table of Contents

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

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Basis of Presentation and Principles of Consolidation

The accompanying condensed consolidated financial statements of Alnylam Pharmaceuticals, Inc. (the Company or Alnylam) are unaudited and have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP) applicable to interim periods and, in the opinion of management, include all normal and recurring adjustments that are necessary to present fairly the results of operations for the reported periods. The Company s condensed consolidated financial statements have also been prepared on a basis substantially consistent with, and should be read in conjunction with, the Company s audited consolidated financial statements for the year ended December 31, 2010, which were included in the Company s Annual Report on Form 10-K that was filed with the Securities and Exchange Commission (the SEC) on February 18, 2011. The year-end condensed balance sheet data was derived from audited financial statements, but does not include all disclosures required by GAAP. The results of the Company s operations for any interim period are not necessarily indicative of the results of the Company s operations for any other interim period or for a full fiscal year.

The accompanying condensed consolidated financial statements reflect the operations of the Company and its wholly-owned subsidiaries, Alnylam U.S., Inc., Alnylam Europe AG (Alnylam Europe) and Alnylam Securities Corporation. All significant intercompany accounts and transactions have been eliminated. The Company uses the equity method of accounting to account for its investment in Regulus Therapeutics Inc. (Regulus).

Use of Estimates

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

Net Loss Per Common Share

Basic net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding. Diluted net loss per common share is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares and dilutive potential common share equivalents then outstanding. Potential common shares consist of shares issuable upon the exercise of stock options (using the treasury stock method), and unvested restricted stock awards. Because the inclusion of potential common shares would be anti-dilutive for all periods presented, diluted net loss per common share is the same as basic net loss per common share.

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

	Three and Six Months Ended June 30,	
	2011	**2010**
Options to purchase common stock	8,925	7,872
Unvested restricted common stock	341	
	9,266	7,872

Restricted Stock Awards

The fair value of restricted stock awards granted to employees is based upon the quoted closing market price per share on the date of grant, adjusted for assumed forfeitures. For performance-based restricted stock awards, the value

of the awards is measured when the Company determines the achievement of such performance conditions are deemed probable. Expense is recognized over the vesting period, commencing when the Company determines that it is probable that the awards will vest. In May 2011, the Company granted an aggregate of 229,806 shares of performance-based restricted stock awards to all employees, excluding the Company s leadership team. These restricted stock awards were valued

Table of Contents

at $2.3 million on the grant date and have a term of five years. The vesting of these awards is predicated on the Company s achievement of certain clinical development goals. For the six months ended June 30, 2011, the Company recorded $0.3 million of stock-based compensation expense related to these restricted stock awards.

Fair Value Measurements

The following tables present information about the Company s assets that are measured at fair value on a recurring basis at June 30, 2011 and December 31, 2010, and indicate the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value. In general, fair values determined by Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities. Fair values determined by Level 2 inputs utilize data points that are observable, such as quoted prices (adjusted), interest rates and yield curves. Fair values determined by Level 3 inputs utilize unobservable data points for the asset or liability, and include situations where there is little, if any, market activity for the asset or liability. Financial assets measured at fair value on a recurring basis are summarized as follows, in thousands:

Description	At June 30, 2011	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	$ 63,962	$ 46,462	$ 17,500	$
Marketable securities (fixed income)				
Corporate notes	119,353		119,353	
U.S. Government obligations	102,036		102,036	
Commercial paper	26,484		26,484	
Marketable securities (equity holdings)	1,046		1,046	
Total	$ 312,881	$ 46,462	$ 266,419	$

Description	At December 31, 2010	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	$ 59,702	$ 40,686	$ 19,016	$
Marketable securities (fixed income)				
Corporate notes	133,341		133,341	
U.S. Government obligations	122,273		122,273	
Commercial paper	17,733		17,733	
Marketable securities (equity holdings)	1,958		1,958	
Total	$ 335,007	$ 40,686	$ 294,321	$

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

Investments in Marketable Securities

The Company invests its excess cash balances in short-term and long-term marketable debt and equity securities. The Company classifies its investments in marketable debt securities as either held-to-maturity or

available-for-sale based on facts and circumstances present at the time it purchased the securities. At each balance sheet date presented, the Company classified all of its investments in debt and equity securities as available-for-sale. The Company reports available-for-sale investments at fair value at each balance sheet date and includes any unrealized holding gains and losses (the adjustment to fair value) in stockholders equity. Realized gains and losses are determined using the specific identification method and are included in other income. If any adjustment to fair value reflects a decline in the value of the investment, the Company considers all available evidence to evaluate the extent to which the decline is other than temporary and, if so, marks the investment to market through a charge to its condensed consolidated statements of operations. The Company did not record any impairment charges related to its fixed income marketable securities during the current period. The Company s marketable securities are classified as cash equivalents if the original maturity, from the date of purchase, is 90 days or less, and as marketable securities if the original maturity, from the date of purchase, is in excess of 90 days. The Company s cash equivalents are composed of money market funds, U.S. government obligations and commercial paper.

The following tables summarize the Company s marketable securities at June 30, 2011 and December 31, 2010, in thousands:

Table of Contents

	June 30, 2011			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper (Due within 1 year)	$ 26,488	$	$ (4)	$ 26,484
Corporate notes (Due within 1 year)	87,255	92	(13)	87,334
Corporate notes (Due after 1 year through 2 years)	32,033	10	(24)	32,019
U.S. Government obligations (Due within 1 year)	37,013	10	(2)	37,021
U.S. Government obligations (Due after 1 year through 2 years)	65,031	13	(29)	65,015
Equity securities	1,345		(299)	1,046
Total	$ 249,165	$ 125	$ (371)	$ 248,919

	December 31, 2010			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Commercial paper (Due within 1 year)	$ 17,734	$ 2	$ (3)	$ 17,733
Corporate notes (Due within 1 year)	116,385	204	(23)	116,566
Corporate notes (Due after 1 year through 2 years)	16,767	33	(25)	16,775
U.S. Government obligations (Due within 1 year)	24,246	1	(14)	24,233
U.S. Government obligations (Due after 1 year through 2 years)	98,111	22	(93)	98,040
Equity securities	1,345	613		1,958
Total	$ 274,588	$ 875	$ (158)	$ 275,305

Subsequent Events

The Company evaluated all events or transactions that occurred after June 30, 2011 up through the date these condensed consolidated financial statements were issued. During this period, the Company did not have any material recognizable or nonrecognizable subsequent events.

Recent Accounting Pronouncements

In January 2011, the Company adopted new authoritative guidance on revenue recognition for multiple element arrangements. The guidance, which applies to multiple element arrangements entered into or materially modified on or after January 1, 2011, amends the criteria for separating and allocating consideration in a multiple element arrangement by modifying the fair value requirements for revenue recognition and eliminating the use of the residual method. The fair value of deliverables under the arrangement may be derived using a best estimate of selling price if vendor specific objective evidence and third-party evidence is not available. Deliverables under the arrangement will be separate units of accounting provided (i) a delivered item has value to the customer on a standalone basis; and (ii) if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the control of the vendor. The Company did not enter into any significant multiple element arrangements or materially modify any existing multiple element arrangements during the six months ended June 30, 2011. The Company s existing license and collaboration agreements continue to be accounted for under previously issued revenue recognition guidance for multiple element arrangements.

In May 2011, the Financial Accounting Standards Board (FASB) issued a new accounting standard that clarifies the application of certain existing fair value measurement guidance and expands the disclosures for fair value

measurements that are estimated using significant unobservable (Level 3) inputs. This new standard is effective on a prospective basis for annual and interim reporting periods beginning on or after December 15, 2011. The Company does not expect that adoption of this new standard will have a material impact on its condensed consolidated financial statements.

In June 2011, the FASB issued a new accounting standard that eliminates the option to present the components of other comprehensive income as part of the statement of changes in stockholders equity, requires the consecutive presentation of the statement of net income and other comprehensive income and requires an entity to present reclassification adjustments on the face of the financial statements from other comprehensive income to net income. The amendments in this new standard do not change the items that must be reported in other comprehensive income or when an item of other comprehensive income must be reclassified to net income nor do the amendments affect how earnings per share is calculated or presented. This new standard is required to be applied retrospectively and is effective for fiscal years and interim periods within those years beginning after December 15, 2011. As this new standard only requires enhanced disclosure, the adoption of this standard will not impact the Company s condensed consolidated financial statements.

Table of Contents

2. SIGNIFICANT AGREEMENTS

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2011	2010	2011	2010
Roche	$ 13,994	$ 13,994	$ 27,988	$ 27,988
Takeda	5,493	5,489	11,261	10,923
Novartis	59	2,614	118	4,973
Other	1,068	4,520	2,144	7,297
Total net revenues from research collaborators	$ 20,614	$ 26,617	$ 41,511	$ 51,181

Platform Alliances

Roche Alliance

In July 2007, the Company and, for limited purposes, Alnylam Europe, entered into a license and collaboration agreement (the LCA) with F. Hoffmann-La Roche Ltd (Roche Basel) and Hoffmann-La Roche Inc. (together with Roche Basel, Roche). Under the LCA, which became effective in August 2007, the Company granted Roche a non-exclusive license to the Company s intellectual property, including delivery-related intellectual property existing as of the date of the LCA, to develop and commercialize therapeutic products that function through RNA interference (RNAi), subject to the Company s existing contractual obligations to third parties. The license is initially limited to four therapeutic areas, and may be expanded to include up to 18 additional therapeutic areas, comprising substantially all other fields of human disease, as identified and agreed upon by the parties, upon payment to the Company by Roche of an additional $50.0 million for each additional therapeutic area, if any.

In consideration for the rights granted to Roche under the LCA, Roche paid the Company $273.5 million in upfront cash payments. In addition, in exchange for the Company s contributions under the LCA, for each RNAi therapeutic product developed by Roche, its affiliates or sublicensees under the LCA, the Company is entitled to receive milestone payments upon achievement of specified development and sales events, totaling up to an aggregate of $100.0 million per therapeutic target, together with royalty payments based on worldwide annual net sales, if any. Under the LCA, the Company and Roche also established a discovery collaboration in October 2009 (Discovery Collaboration), subject to the Company s existing contractual obligations to third parties.

In July 2007, the Company executed a common stock purchase agreement (the Common Stock Purchase Agreement) with Roche Finance Ltd, an affiliate of Roche. In connection with the execution of the LCA and the Common Stock Purchase Agreement, the Company also executed a share purchase agreement (the Alnylam Europe Purchase Agreement) with Alnylam Europe and Roche Beteiligungs GmbH, an affiliate of Roche (Roche Germany). Under the terms of the Alnylam Europe Purchase Agreement, the Company sold substantially all of the non-intellectual property assets of Alnylam Europe to Roche Germany for an aggregate purchase price of $15.0 million.

In summary, the Company received upfront payments totaling $331.0 million under the Roche alliance, which include an upfront payment under the LCA of $273.5 million, $42.5 million under the Common Stock Purchase Agreement and $15.0 million under the Alnylam Europe Purchase Agreement. The Company initially recorded $278.2 million of these proceeds as deferred revenue in connection with the Roche alliance.

When evaluating multiple element arrangements, the Company considers whether the components of the arrangement represent separate units of accounting. The accounting guidance specifically requires that the delivered components must have value to the customer on a standalone basis and that there is objective and reliable evidence of the fair value of the undelivered components. Application of this standard requires subjective determinations and requires management to make judgments about the value of each individual element and whether it is separable from the other aspects of the contractual relationship. The Company has determined that the deliverables under its

agreements with Roche include the license, the Alnylam Europe assets and employees, the steering committees (joint steering committee and future technology committee) and the services under the Discovery Collaboration. The Company has determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the license and assets of Alnylam Europe are not separable from the undelivered services (i.e., the steering committees and Discovery

Table of Contents

Collaboration) and, accordingly the license and the services are being treated as a single unit of accounting. When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition pattern on the final deliverable. Under the Roche alliance, the steering committee services and the Discovery Collaboration services are the final deliverables and all such services will end, contractually, five years from the effective date of the LCA.

In November 2010, Roche announced the discontinuation of certain activities in research and early development, including its RNAi research efforts. The remaining deliverables under the LCA currently remain in effect. Roche may assign its rights and obligations under the LCA to a third party in connection with the sale or transfer of its entire RNAi business.

The Company is recognizing the Roche-related revenue on a straight-line basis over five years because the Company cannot reasonably estimate the total level of effort required to complete its service obligations under the LCA, and therefore, cannot utilize a proportional performance model. As future substantive milestones are achieved, the Company will recognize as revenue a portion of the milestone payment, equal to the percentage of the performance period completed when the milestone is achieved, multiplied by the amount of the milestone payment. The Company will recognize the remaining portion of the milestone over the remaining performance period on a straight-line basis. The Company will continue to recognize the Roche-related revenue on a straight-line basis over five years. If Roche terminates the LCA or assigns its rights and obligations thereunder to a third party, at such time, the Company will reassess its deliverables and the period over which it will complete its performance obligations under the LCA. At June 30, 2011, deferred revenue under the LCA was $65.3 million.

Takeda Alliance

In May 2008, the Company entered into a license and collaboration agreement (the Takeda Collaboration Agreement) with Takeda Pharmaceutical Company Limited (Takeda) to pursue the development and commercialization of RNAi therapeutics. Under the Takeda Collaboration Agreement, the Company granted Takeda a non-exclusive, worldwide, royalty-bearing license to the Company s intellectual property, including delivery-related intellectual property, controlled by the Company as of the date of the agreement or during the five years thereafter, to develop, manufacture, use and commercialize RNAi therapeutics, subject to the Company s existing contractual obligations to third parties. The license initially is limited to the fields of oncology and metabolic disease and may be expanded at Takeda s option to include other therapeutic areas, subject to specified conditions. Under the Takeda Collaboration Agreement, Takeda is the Company s exclusive platform partner in the Asian territory, as defined in the Takeda Collaboration Agreement through May 2013.

In consideration for the rights granted to Takeda under the Takeda Collaboration Agreement, Takeda agreed to pay the Company $150.0 million in upfront and near-term technology transfer payments. In addition, the Company has the option, exercisable until the start of Phase III development, to opt-in under a 50-50 profit sharing agreement to the development and commercialization in the United States of up to four Takeda licensed products, and would be entitled to opt-in rights for two additional products for each additional field expansion, if any, elected by Takeda under the Takeda Collaboration Agreement. In June 2008, Takeda paid the Company an upfront payment of $100.0 million and agreed to pay an additional $50.0 million to the Company upon achievement of specified technology transfer milestones. Of this $50.0 million, $20.0 million was paid to the Company in October 2008, $20.0 million was paid to the Company in March 2010 and $10.0 million was paid to the Company in March 2011 (collectively, Technology Transfer Milestones). If Takeda elects to expand its license to additional therapeutic areas, Takeda will be required to pay the Company $50.0 million for each of up to approximately 20 total additional fields selected, if any, comprising substantially all other fields of human disease, as identified and agreed upon by the parties. In addition, for each RNAi therapeutic product developed by Takeda, its affiliates and sublicensees, the Company is entitled to receive specified development and commercialization milestones, totaling up to $171.0 million per product, together with royalty payments based on worldwide annual net sales, if any.

Pursuant to the Takeda Collaboration Agreement, the Company and Takeda are also collaborating on the research of RNAi therapeutics directed to one or two disease targets agreed to by the parties (the Research Collaboration), subject to the Company s existing contractual obligations with third parties. Takeda also has the option, subject to certain conditions, to collaborate with the Company on the research and development of RNAi drug

delivery technology for targets agreed to by the parties. In addition, Takeda has a right of first negotiation for the development and commercialization of the Company s RNAi therapeutic products in the Asian territory, excluding the Company s ALN-RSV program. In addition to the 50-50 profit sharing option, the Company has a similar right of first negotiation to participate with Takeda in the development and commercialization in the United States of licensed products. The collaboration is governed by a joint technology transfer committee (the JTTC), a joint research collaboration committee (the JRCC) and a joint delivery collaboration committee (the JDCC), each of which is comprised of an equal number of representatives from each party.

Table of Contents

The Company has determined that the deliverables under the Takeda Collaboration Agreement include the license, the joint committees (the JTTC, JRCC and JDCC), the technology transfer activities and the services that the Company will be obligated to perform under the Research Collaboration. The Company has determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the license and undelivered services (i.e., the joint committees and the Research Collaboration) are not separable and, accordingly, the license and services are being treated as a single unit of accounting. When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition pattern on the final deliverable. Under the Takeda Collaboration Agreement, the last elements to be delivered are the JDCC and JTTC services, each of which has a life of no more than seven years.

The Company is recognizing the upfront payment of $100.0 million and the Technology Transfer Milestones of $50.0 million, the receipt of which the Company believed was probable at the commencement of the collaboration, on a straight-line basis over seven years because the Company is unable to reasonably estimate the level of effort to fulfill these obligations, primarily because the effort required under the Research Collaboration is largely unknown, and therefore, cannot utilize the proportional performance model. As future substantive milestones are achieved, the Company will recognize as revenue a portion of the milestone payment equal to the percentage of the performance period completed when the milestone is achieved, multiplied by the amount of the milestone payment. The Company will recognize the remaining portion of the milestone over the remaining performance period on a straight-line basis. At June 30, 2011, deferred revenue under the Takeda Collaboration Agreement was $85.8 million.

Discovery and Development Alliances

Novartis Broad Alliance

In the second half of 2005, the Company entered into a series of transactions with Novartis Pharma AG and its affiliate, Novartis Institutes for BioMedical Research, Inc. (together, Novartis), which included a stock purchase agreement, an investor rights agreement (the Investor Rights Agreement), and a research collaboration and license agreement (the Collaboration and License Agreement). The Collaboration and License Agreement had an initial research term of three years, with an option for two additional one-year extensions at the election of Novartis. Novartis elected to extend the term through October 2010, the fifth and final planned year. In October 2010, the research program under the Collaboration and License Agreement was substantially completed in accordance with the terms of the Collaboration and License Agreement, subject to certain surviving rights and obligations of the parties.

The Investor Rights Agreement provides Novartis with the right generally to maintain its ownership percentage in the Company until the earlier of any sale by Novartis of shares of the Company s common stock and the expiration or termination of the Collaboration and License Agreement, subject to certain exceptions. At June 30, 2011, Novartis owned 13.1% of the Company s outstanding common stock.

In consideration for the rights granted to Novartis under the Collaboration and License Agreement, Novartis made an upfront payment of $10.0 million to the Company in October 2005, partly to reimburse prior costs incurred by the Company to develop *in vivo* RNAi technology. The Company also received research funding and development milestone payments from Novartis.

In September 2010, Novartis exercised its right under the Collaboration and License Agreement to select 31 designated gene targets, for which Novartis has exclusive rights to discover, develop and commercialize RNAi therapeutic products using the Company s intellectual property and technology, including delivery-related intellectual property and related technology. Under the terms of the Collaboration and License Agreement, for any RNAi therapeutic products Novartis develops against these targets, the Company is entitled to receive milestone payments upon achievement of certain specified development and annual net sales events, up to an aggregate of $75.0 million per therapeutic product, as well as royalties on annual net sales of any such product. Novartis right of first offer with respect to an exclusive license for additional targets has terminated. In September 2010, Novartis declined to exercise its non-exclusive option to integrate into its operations the Company s fundamental and chemistry intellectual property under the terms of the Collaboration and License Agreement. If Novartis had elected to exercise the integration option, Novartis would have been required to make additional payments to the Company totaling $100.0 million.

The Company believes the estimated period of performance under the Collaboration and License Agreement is ten years, which includes the three-year initial term of the agreement, two one-year extensions elected by Novartis and

limited support as part of a technology transfer until 2015, the fifth anniversary of the completion of the research term under the Collaboration and License Agreement. The Company continues to use an expected term of ten years in its proportional performance model. The Company reevaluates the expected term when new information is known that could affect the Company s estimate. In the event the Company s period of performance is different than estimated, the Company will adjust the amount of revenue recognized on a prospective basis.

Table of Contents

At June 30, 2011, deferred revenue under the Novartis Collaboration and License Agreement was $0.3 million.

Product Alliances

Kyowa Hakko Kirin Alliance

In June 2008, the Company entered into a license and collaboration agreement (the Kyowa Hakko Kirin Agreement) with Kyowa Hakko Kirin Co., Ltd. (Kyowa Hakko Kirin). Under the Kyowa Hakko Kirin Agreement, the Company granted Kyowa Hakko Kirin an exclusive license to its intellectual property in Japan and other markets in Asia (the Licensed Territory) for the development and commercialization of an RNAi therapeutic for the treatment of respiratory syncytial virus (RSV) infection. The Kyowa Hakko Kirin Agreement covers ALN-RSV01, as well as additional RSV-specific RNAi therapeutic compounds that comprise the ALN-RSV program (Additional Compounds). The Company retains all development and commercialization rights worldwide outside of the Licensed Territory, subject to its agreement with Cubist Pharmaceuticals, Inc. (Cubist) described below.

Under the terms of the Kyowa Hakko Kirin Agreement, in June 2008, Kyowa Hakko Kirin paid the Company an upfront cash payment of $15.0 million. In addition, Kyowa Hakko Kirin is required to make payments to the Company upon achievement of specified development and sales milestones totaling up to $78.0 million, and royalty payments based on annual net sales, if any, of RNAi therapeutics for the treatment of RSV by Kyowa Hakko Kirin, its affiliates and sublicensees in the Licensed Territory.

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

The Company has determined that the deliverables under the Kyowa Hakko Kirin Agreement include the license, the joint steering committee, the manufacturing services and any Additional Compounds. The Company has determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the individual deliverables are not separable and, accordingly, must be accounted for as a single unit of accounting. When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition pattern on the final deliverable. The Company is currently unable to reasonably estimate its period of performance under the Kyowa Hakko Kirin Agreement, as it is unable to estimate the timeline of its deliverables related to the fixed-price option granted to Kyowa Hakko Kirin for any Additional Compounds. The Company is deferring all revenue under the Kyowa Hakko Kirin Agreement until it is able to reasonably estimate its period of performance. The Company will continue to reassess whether it can reasonably estimate the period of performance to fulfill its obligations under the Kyowa Hakko Kirin Agreement. At June 30, 2011, deferred revenue under the Kyowa Hakko Kirin Agreement was $15.5 million.

Cubist Alliance

In January 2009, the Company entered into a license and collaboration agreement with Cubist (the Cubist Agreement) to develop and commercialize therapeutic products (Licensed Products) based on certain of the Company s RNAi technology for the treatment of RSV infection. Licensed Products initially included ALN-RSV01, as well as several other second-generation RNAi-based RSV inhibitors. In November 2009, the Company and Cubist entered into an amendment to the Cubist Agreement (the Amendment), which provides that the Company and Cubist would focus their collaboration and joint development efforts on ALN-RSV02, a second-generation compound, intended for use in pediatric patients. Consistent with the original Cubist Agreement, the Company and Cubist were each responsible for one-half of the related development costs for ALN-RSV02. Pursuant to the terms of the Amendment, the Company is continuing to develop ALN-RSV01 for adult transplant patients at its sole discretion and expense. Cubist has the right to opt into collaborating with the Company on ALN-RSV01 in the future, which right may be exercised for a specified period of time following the completion of the Company s Phase IIb trial of ALN-RSV01,

subject to the payment by Cubist of an opt-in fee representing reimbursement of an agreed upon percentage of certain of the Company s development expenses for ALN-RSV01. In December 2010, the Company and Cubist jointly made a portfolio decision to put the development of ALN-RSV02 on hold.

In consideration for the rights granted to Cubist under the Cubist Agreement, in January 2009, Cubist paid the Company an

Table of Contents

upfront cash payment of $20.0 million. Cubist is also obligated under the Cubist Agreement to pay the Company milestone payments, totaling up to an aggregate of $82.5 million, and has the right to convert the North American co-development and profit sharing arrangement into a royalty-bearing license.

The Company has determined that the deliverables under the Cubist Agreement include the licenses, technology transfer related to the ALN-RSV program, the joint steering committee and the development and manufacturing services that the Company is obligated to perform during the development period. The Company also has determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the licenses and undelivered services are not separable and, accordingly, the licenses and services are being treated as a single unit of accounting. When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition pattern on the final deliverable. Under the Cubist Agreement, the last element to be delivered is the development and manufacturing services, which have an expected life of approximately eight years.

The Company is recognizing the upfront payment of $20.0 million on a straight-line basis over approximately eight years because the Company is unable to reasonably estimate the level of effort to fulfill its performance obligations, and therefore, cannot utilize a proportional performance model. As future substantive milestones are achieved, the Company will recognize as revenue a portion of the milestone payment, equal to the percentage of the performance period completed when the milestone is achieved, multiplied by the amount of the milestone payment. The Company will recognize the remaining portion of the milestone over the remaining performance period on a straight-line basis. At June 30, 2011, deferred revenue under the Cubist Agreement was $13.8 million.

Under the terms of the Cubist Agreement, the Company and Cubist share responsibility for developing Licensed Products in North America and each bears one-half of the related development costs, provided that under the terms of the Amendment, the Company is funding the advancement of ALN-RSV01 for adult lung transplant patients and Cubist retains an opt-in right. For revenue generating arrangements that involve cost sharing between the parties, the Company presents the results of activities for which it acts as the principal on a gross basis and reports any payments received from, or made to, other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, analogy to authoritative accounting literature or a reasonable, rational and consistently applied accounting policy election. As the Company is not considered the principal under the Cubist Agreement, the Company records any amounts due from Cubist as a reduction of research and development expense.

3. INCOME TAXES

The Company expects to generate U.S. taxable losses during 2011 and has recorded no income tax provision for the three or six months ended June 30, 2011. During each of the three and six months ended June 30, 2010, the Company recorded a benefit from income taxes of $0.2 million.

During 2009 and 2008, the Company utilized certain tax attributes, including net operating loss and tax credit carryforwards as a result of the recognition of revenue for certain proceeds received from strategic alliances. However, the Company also generated a deferred tax asset related to the recognition of this revenue for tax purposes and recorded a net deferred tax asset to the extent it was more likely than not that the asset would be realized. During 2010, the Company generated sufficient net operating losses to carry back to 2009 and 2008 to obtain a refund of taxes paid in those years, resulting in a realization of its net deferred tax asset. As a result, during 2010, the Company reclassified $10.7 million of its deferred tax asset to income taxes receivable. The Company received this income tax refund during the three months ended March 31, 2011.

At December 31, 2010, the Company had federal and state net operating loss carryforwards of $27.5 million and $101.6 million, respectively, to reduce future taxable income that will expire at various dates through 2030. Ownership changes, as defined in the Internal Revenue Code, including those resulting from the issuance of common stock in connection with the Company s public offerings, may limit the amount of net operating loss that can be utilized to offset future taxable income or tax liability. The Company has determined that there is no limitation on the utilization of net operating loss carryforwards in accordance with Section 382 of the Internal Revenue Code. In July 2011, the Internal Revenue Service completed its audits of the Company s 2008 and 2009 tax years. The Company did not record any tax expense related to these audits.

The Company continues to recognize fully its tax benefits which are offset by a valuation allowance to the extent that it is more likely than not that the deferred tax assets will not be realized. At June 30, 2011, the Company

had $0.1 million of total gross unrecognized tax benefits that, if recognized, would favorably impact the Company s effective income tax rate in future periods.

Table of Contents

4. REGULUS

In September 2007, the Company and Isis Pharmaceuticals, Inc. (Isis) established Regulus, a company focused on the discovery, development and commercialization of microRNA therapeutics, a potential new class of drugs to treat the pathways of human disease. Regulus, which initially was established as a limited liability company, converted to a C corporation in January 2009 and changed its name to Regulus Therapeutics Inc.

In consideration for the Company s and Isis initial interests in Regulus, each party granted Regulus exclusive licenses to its intellectual property for certain microRNA therapeutic applications as well as certain patents in the microRNA field. In addition, the Company made an initial cash contribution to Regulus of $10.0 million, resulting in the Company and Isis making approximately equal aggregate initial capital contributions to Regulus. In March 2009, the Company and Isis each purchased $10.0 million of Series A preferred stock of Regulus. In October 2010, in connection with its strategic alliance with Regulus formed in June 2010, Sanofi made a $10.0 million equity investment in Regulus. As a result of this investment, the Company recognized a gain of $4.4 million due to the increase in valuation of Regulus. This amount was recorded as other income in the Company s consolidated statements of operations for the year ended December 31, 2010. At June 30, 2011, the Company, Isis and Sanofi owned approximately 45%, 46% and 9%, respectively, of Regulus. Regulus continues to operate as an independent company with a separate board of directors, scientific advisory board and management team, some of whom have options to purchase common stock of Regulus. Members of the board of directors of Regulus who are the Company s employees or Isis employees are not eligible to receive options to purchase Regulus common stock.

The Company has reviewed the consolidation guidance that defines a variable interest entity (VIE) and concluded that Regulus currently qualifies as a VIE. The Company does not consolidate Regulus as the Company lacks the power to direct the activities that could significantly impact the economic success of this entity. At June 30, 2011, the total carrying value of the Company s investment in joint venture (Regulus Therapeutics Inc.) in its condensed consolidated balance sheets was $1.8 million under the equity method. The Company s maximum exposure to loss related to this VIE is limited to the carrying value of the Company s investment, as well the portion of Regulus debt, including accrued interest, guaranteed by the Company which was $5.4 million at June 30, 2011.

The Company accounts for its investment in Regulus using the equity method of accounting. Summary results of Regulus operations for the three and six months ended June 30, 2011 and 2010 and balance sheets at June 30, 2011 and December 31, 2010 are presented in the tables below, in thousands (unaudited):

	Three Months Ended June 30,		Six Months Ended June 30,	
	2011	2010	2011	2010
Statement of Operations Data:				
Net revenues	$ 3,308	$ 809	$ 6,617	$ 1,495
Operating expenses	5,446	8,685	10,905	12,439
Loss from operations	(2,138)	(7,876)	(4,288)	(10,944)
Other expense	(116)	(54)	(255)	(84)
Net loss	$ (2,254)	$ (7,930)	$ (4,543)	$ (11,028)

	June 30, 2011	December 31, 2010
Balance Sheet Data:		
Cash, cash equivalents and marketable securities	$ 42,616	$ 54,789
Working capital	29,887	40,446
Total assets	47,546	59,703

Notes payable	11,265	11,270
Total stockholders equity	3,881	7,996

Table of Contents

5. COMMITMENTS AND CONTINGENCIES

Litigation

Tekmira Litigation

On March 16, 2011, Tekmira Pharmaceuticals Corporation and Protiva Biotherapeutics, Inc. filed a civil complaint in the Business Litigation Section of the Suffolk County Superior Court, in Boston, Massachusetts against the Company and on June 3, 2011, the plaintiffs filed an amended complaint adding AlCana Technologies, Inc. (AlCana), a research collaborator of the Company, as a defendant. The amended complaint alleges misappropriation of the plaintiffs confidential and proprietary information and trade secrets, civil conspiracy, and tortious interference with contractual relationships by the Company and AlCana, and unjust enrichment, contractual breach, breach of the implied covenant of good faith and fair dealing, unfair competition, false advertising, and unfair and deceptive acts and practices by the Company, and seeks injunctive relief and unspecified damages and other relief. On April 6, 2011, the Company timely served and filed an answer to the plaintiffs original complaint denying the plaintiffs claims in this action, together with counterclaims against the plaintiffs. On June 28, 2011, the Company timely served and filed an answer to the plaintiffs amended complaint denying the plaintiffs claims and counterclaims against the plaintiffs asserting breach of contract, defamation, breach of covenant not to sue, breach of patent prosecution and non-use provisions, misappropriation of confidential and proprietary information and trade secrets, unjust enrichment, breach of the implied covenant of good faith and fair dealing, as well as violations of Massachusetts statutes. The Company is seeking the dismissal of plaintiffs claims and judgment in its favor, as well as damages and equitable relief.

University of Utah Litigation

On March 22, 2011, The University of Utah (the University) filed a civil complaint in the United States District Court for the District of Massachusetts against the Company, Max Planck Gesellschaft Zur Forderung Der Wissenschaften E.V. and Max Planck Innovation GmbH (together, Max Planck), the Whitehead Institute for Biomedical Research (Whitehead), the Massachusetts Institute of Technology (MIT) and the University of Massachusetts (UMass), claiming a professor at the University is the sole inventor or, in the alternative, a joint inventor, of the Tuschl patents. The University did not serve the original complaint on the Company or the other defendants. On July 6, 2011, the University filed an amended complaint alleging substantially the same claims against the Company, Max Planck, Whitehead, MIT and UMass. The amended complaint was served on the Company on July 14, 2011. The University is seeking changes to the inventorship of the Tuschl patents, unspecified damages and other relief.

Although the Company believes that it has meritorious defenses to each of the claims in the lawsuits described above and intends to fully defend itself in these matters, litigation is subject to inherent uncertainty and a court could ultimately rule against the Company in one or both of these matters. In addition, the defense of litigation and related matters are costly and may divert the attention of the Company s management and other resources that would otherwise be engaged in running the Company s business. The Company has not recorded an estimated liability associated with the legal proceedings described above due in each case to the uncertainties related to both the likelihood and the amount of any potential loss.

Tuschl Settlement

In March 2011, the Company, Max Planck, Whitehead and UMass entered into a global settlement agreement (the Settlement Agreement) resolving their ongoing litigation regarding the Tuschl patents. MIT, formerly a party to the litigation, also agreed to the terms of the Settlement Agreement.

The litigation was initiated in June 2009 and scheduled for trial in March 2011 in the United States District Court for the District of Massachusetts, and related to, among other things, the prosecution of the Tuschl I and Tuschl II patent applications. In the field of RNAi therapeutics, the Company is the exclusive licensee of the Tuschl I patent applications from Max Planck, MIT and Whitehead, and of the Tuschl II patent applications from Max Planck. The terms of the Settlement Agreement included mutual releases and dismissal with prejudice of all claims and counterclaims in the litigation between the parties.

As part of the Settlement Agreement, Max Planck, Whitehead, UMass and MIT agreed that future prosecution of the Tuschl I and Tuschl II patent families in the United States should be coordinated and led by a single party. Max Planck will assume that role, in addition to their ongoing leadership in the continued prosecution of the Tuschl II

patent family outside the United States. UMass will lead future prosecution of the Tuschl I patent family outside the United States. In addition, under the terms of the Settlement Agreement, the Company granted UMass the right to sublicense the U.S. Tuschl II patent family to Merck & Co., Inc., subject to certain third-party obligations of the Company and other limitations, in exchange for a share of certain future sublicense income.

The Company incurred costs of $3.3 million and $3.8 million during the three months ended March 31, 2011 and 2010, respectively, in connection with this dispute. These costs were charged to general and administrative expense. The Company does not expect to incur any additional significant expenses related to this dispute.

6. RESTRUCTURING

In September 2010, as a result of the planned completion of the fifth and final year of the research program under the Novartis Collaboration and License Agreement and the Company s reduced need for service-based collaboration resources, the Company s Board of Directors approved and the Company effected a corporate restructuring to focus the Company s resources on its most promising programs and significantly reduce its cost structure. The corporate restructuring included implementing a reduction of the Company s overall workforce by approximately 25%.

During the year ended December 31, 2010, the Company recorded $2.2 million of restructuring-related costs in operating expenses, including employee severance, benefits and related costs. During the six months ended June 30, 2011, the Company did not record any additional restructuring related costs.

The following table summarizes the components of the Company s restructuring expenses recorded in operating expenses and in current liabilities, in thousands:

	Original Charges and Amounts Accrued	(Reversals) or Adjustments to Charges	Amounts Paid Through June 30, 2011	Amounts Accrued at June 30, 2011
Employee severance, benefits and related costs	$ 2,193	$ (20)	$ 2,113	$ 60
Total	$ 2,193	$ (20)	$ 2,113	$ 60

Table of Contents

The following table summarizes the components of the Company s restructuring activities for the six months ended June 30, 2011, in thousands:

	Amounts Accrued at December 31, 2010	(Reversals) or Adjustments to Charges	Amounts Paid Through June 30, 2011	Amounts Accrued at June 30, 2011
Employee severance, benefits and related costs	$ 977	$	$ 917	$ 60
Total	$ 977	$	$ 917	$ 60

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, goal and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these words. 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 to reflect events or circumstances that arise after the date hereof. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of certain important factors, including those set forth below under this Item 2 Management s Discussion and Analysis of Financial Condition and Results of Operations, Part II, Item 1A Risk Factors and elsewhere in this Quarterly Report on Form 10-Q. You should carefully review those factors and also carefully review the risks outlined in other documents that we file from time to time with the Securities and Exchange Commission, or SEC.

Overview

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

Our core product strategy, which we refer to as Alnylam 5x15, is focused on the development and commercialization of innovative RNAi therapeutics for the treatment of genetically defined diseases. Under our core product strategy, we expect to progress five RNAi therapeutic programs into advanced stages of clinical development by the end of 2015. As part of this strategy, our goal is to develop product candidates with the following shared characteristics: a genetically defined target and disease; the potential to have a significant impact in high unmet need patient populations; the ability to leverage our existing RNAi delivery platform; the opportunity to monitor an early biomarker in Phase I clinical trials for human proof of concept; and the existence of clinically relevant endpoints for the filing of a new drug application, or NDA, with a focused patient database and possible accelerated paths for commercialization. We intend to commercialize products arising from this core product strategy on our own in the United States and potentially certain other countries, and we intend to enter into alliances to develop and commercialize any such products in other global territories. We are currently advancing three core programs in clinical or pre-clinical development: ALN-TTR for the treatment of transthyretin-mediated amyloidosis, or ATTR; ALN-PCS for the treatment of severe hypercholesterolemia; and ALN-HPN for the treatment of refractory anemia. As part of our core product strategy, we also expect to designate and start pre-clinical development of two additional RNAi therapeutic candidates targeting genetically defined diseases by the end of 2011.

While focusing our efforts on our core product strategy, we also intend to continue to advance additional development programs through existing or future alliances. We have three partner-based programs in clinical or pre-clinical development, including ALN-RSV01 for the treatment of respiratory syncytial virus, or RSV, infection, ALN-VSP for the treatment of liver cancers and ALN-HTT for the treatment of Huntington s disease, or HD.

Our most advanced core product development program, ALN-TTR, targets the transthyretin, or TTR, gene, for the treatment of ATTR, a hereditary, systemic disease associated with severe morbidity and mortality caused by a mutation in the TTR gene that leads to the extracellular deposition of amyloid fibrils. In July 2010, we initiated a Phase I clinical trial for ALN-TTR01, a systemically delivered RNAi therapeutic. ALN-TTR01 employs a first-generation lipid nanoparticle, or LNP, formulation. The Phase I clinical trial for ALN-TTR01 is being conducted

in Portugal, Sweden, the United Kingdom and France, and is a randomized, blinded, placebo-controlled dose escalation study. As a result of favorable safety data to date, we received regulatory approval to extend this Phase I clinical trial with additional dose cohorts up to 1.0 mg/kg, increasing enrollment from 28 to up to 36 patients. The primary objective is to evaluate the safety and tolerability of a single dose of intravenous ALN-TTR01. Secondary objectives include characterization of plasma and urine pharmacokinetics of ALN-TTR01 and assessment of pharmacodynamic activity based on measurements of circulating TTR serum levels. In January 2011, The Committee for Orphan Medicinal Products of the European

Table of Contents

Medicines Agency adopted a positive opinion for ALN-TTR01 designation as an orphan medicinal product for the treatment of familial amyloidotic polyneuropathy, one of the predominant forms of ATTR. In April 2011, the European Commission officially designated ALN-TTR01 as an orphan drug. In parallel with the development of ALN-TTR01, we are also advancing ALN-TTR02 utilizing a proprietary second-generation LNP formulation.

Our second core product development program is ALN-PCS. ALN-PCS employs a proprietary second-generation LNP formulation, specifically using the MC3 lipid. We are developing ALN-PCS, a systemically delivered RNAi therapeutic, for the treatment of severe hypercholesterolemia. ALN-PCS targets a gene called proprotein convertase subtilisin/kexin type 9, or PCSK9, which is involved in the regulation of LDL receptor levels on hepatocytes and the metabolism of LDL cholesterol, or LDL-c, which is also commonly referred to as bad cholesterol. In July 2011, we filed a clinical trial application, or CTA, with the Medicines and Healthcare products Regulatory Agency, or MHRA, to initiate a Phase I clinical trial for ALN-PCS in the United Kingdom. Upon receiving clearance of the CTA, we plan to initiate the Phase I clinical trial as a randomized, single-blind, placebo-controlled, single ascending dose study, enrolling approximately 32 healthy volunteer subjects with elevated baseline LDLc. The primary objective of the study is to evaluate the safety and tolerability of a single dose of ALN-PCS, with patients being enrolled into five sequential cohorts of increasing doses ranging from 0.015 to 0.25 mg/kg. Secondary objectives include characterization of plasma and urine pharmacokinetics of ALN-PCS, and assessment of pharmacodynamic effects of the drug on plasma PCSK9 protein and LDLc levels measured from serial blood samples prior to and following dosing. Pre-clinical studies with ALN-PCS demonstrated specific silencing of PCSK9 messenger RNA, or mRNA, in the liver, and plasma PCSK9 protein levels of up to 90%, with an ED50 (the dose that provides a 50% silencing effect) of approximately 0.06 mg/kg for both mRNA and protein reduction. These studies have also demonstrated a greater than 50% reduction in levels of LDL-c, which result is rapidly achieved and durable, lasting for weeks after a single dose.

We have designated ALN-HPN as our third core product development program. ALN-HPN is a systemically delivered RNAi therapeutic targeting hepcidin, a genetically validated gene in iron homeostasis, for the treatment of refractory anemia. Anemia of chronic disease, or ACD, occurs in patients with end-stage renal disease, cancer and chronic inflammatory disease. ACD patients who are refractory to erythropoiesis-stimulating agents and intravenous iron define a condition of refractory anemia for which there is substantial unmet need. Pre-clinical studies with a small interfering RNA, or siRNA, targeting hepcidin demonstrated the ability to silence the gene and increase serum iron levels. ALN-HPN also employs a second-generation LNP formulation.

As noted above, while focusing our efforts on our core product strategy, we also intend to continue to advance additional partner-based development programs, including ALN-RSV, ALN-VSP and ALN-HTT, through existing or future alliances.

In February 2010, we initiated a multi-center, global, randomized, double-blind, placebo-controlled Phase IIb clinical trial to evaluate the clinical efficacy as well as safety of aerosolized ALN-RSV01 in adult lung transplant patients naturally infected with RSV. Patients are being randomized in a one-to-one drug to placebo ratio. The primary endpoint of this clinical trial is a reduction in the incidence of new or progressive bronchiolitis obliterans syndrome, or BOS, a potentially life-threatening complication in lung transplant patients. During 2011, we amended the protocol of this clinical trial to perform an interim analysis, blinded to us and investigators, which could expand enrollment from 76 to up to 120 patients. The interim analysis will be performed when 75% of patients are evaluable for the BOS endpoint at six months. We have formed collaborations with Cubist Pharmaceuticals, Inc., or Cubist, and Kyowa Hakko Kirin Co., Ltd., or Kyowa Hakko Kirin, for the development and commercialization of RNAi products for the treatment of RSV. Under our agreement with Cubist, we are developing ALN-RSV01 for adult transplant patients at our sole discretion and expense and Cubist has the right to opt into collaborating with us on ALN-RSV01 in the future. In December 2010, we and Cubist jointly made a portfolio decision to put the development of ALN-RSV02, a second-generation compound for the pediatric population, on hold.

In August 2011, we announced that we have completed a Phase I clinical trial for ALN-VSP, which was our first systemically delivered RNAi therapeutic to enter clinical development. ALN-VSP is comprised of two siRNAs, one targeting vascular endothelial growth factor, or VEGF, and the other targeting kinesin spindle protein, or KSP, and employs a first-generation LNP formulation. We are developing ALN-VSP for the treatment of liver cancers,

including both primary and secondary liver cancers. This Phase I clinical trial was a multi-center, open label, dose escalation study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of intravenous ALN-VSP in patients with advanced solid tumors with liver involvement. We completed enrollment in this clinical trial during the first quarter of 2011 and reported study results in June 2011. ALN-VSP was administered to 41 patients at doses ranging from 0.1 to 1.5 mg/kg and was generally well tolerated. As of July 2011, five patients with disease control were continuing to receive therapy in an extension study. Results from pharmacodynamic measurements provide evidence of biological activity, and biopsy data demonstrate both tissue levels of ALN-VSP and also human proof-of-concept for an RNAi mechanism of action. We intend to partner our ALN-VSP program prior to initiating a Phase II clinical trial.

Table of Contents

A third partner-based development program is ALN-HTT, an RNAi therapeutic candidate targeting the huntingtin gene, for the treatment of HD, which we are developing in collaboration with Medtronic, Inc., or Medtronic. In November 2010, we and Medtronic entered into an agreement with CHDI Foundation, Inc., or CHDI, under which CHDI has agreed to initially fund approximately 50% of the costs of this program up to the point at which an investigational new drug application, or IND, can be filed with the United States Food and Drug Administration, or FDA, or a comparable foreign regulatory filing can be made.

We also continue to work internally and with third-party collaborators to develop new technologies to deliver our RNAi therapeutics both directly to specific sites of disease, and systemically by intravenous or subcutaneous administration. We have numerous RNAi therapeutic delivery collaborations and intend to continue to collaborate with government, academic and corporate third parties to evaluate different delivery options.

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

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

We also seek to form or advance new ventures and opportunities in areas outside our primary focus on RNAi therapeutics. For example, we have presented data regarding the application of RNAi technology to improve the manufacturing processes for biologics, including recombinant proteins and monoclonal antibodies. We are advancing these applications of RNAi technology in an internal effort referred to as Alnylam Biotherapeutics. We have formed, and intend to form additional, collaborations through this effort with third-party biopharmaceutical companies. Additionally, in 2007, we and Isis established Regulus Therapeutics Inc., or Regulus, a company focused on the discovery, development and commercialization of microRNA therapeutics. Because microRNAs are believed to regulate whole networks of genes that can be involved in discrete disease processes, microRNA therapeutics represent a possible new approach to target the pathways of human disease. Regulus has formed collaborations with GlaxoSmithKline, or GSK, and Sanofi to advance its efforts. Given the broad applications for RNAi technology, in addition to our efforts on Alnylam Biotherapeutics and Regulus, we believe new ventures and opportunities will be available to us.

To date, a substantial portion of our total net revenues has been derived from collaboration revenues from strategic alliances with Roche, Takeda, Cubist and Novartis, and from the United States government in connection with our development of treatments for hemorrhagic fever viruses, including Ebola. We expect our revenues to continue to be derived primarily from existing alliances, including those with Roche and Takeda, new strategic alliances, government and foundation funding and license fee revenues.

We have incurred significant losses since we commenced operations in 2002 and expect such losses to continue for the foreseeable future. Historically, we have generated losses principally from costs associated with research and development activities, acquiring, filing and expanding intellectual property rights and general administrative costs. As a result of planned expenditures for research and development activities relating to our drug development

programs, including the development of drug delivery technologies and clinical trial costs, extension of the capabilities of our technology platform, including through business initiatives, continued management and growth of our patent portfolio, collaborations and general corporate activities, we expect to incur additional operating losses for the foreseeable future.

Although we currently have programs focused on a number of therapeutic areas, we are unable to predict when, if ever, we will successfully develop or be able to commence sales of any product. Our sources of potential funding for the next several years are

Table of Contents

expected to be derived primarily from new and existing strategic alliances, which may include license and other fees, funded research and development and milestone payments, government and foundation funding, and proceeds from the sale of equity or debt. In July 2011, we filed a shelf registration statement with the SEC for an indeterminate number of shares of common stock and/or other securities, up to an aggregate of $150 million, for future issuance.

We anticipate that our operating results will fluctuate for the foreseeable future and, therefore, period-to-period comparisons should not be relied upon as predictive of the results of future periods.

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. Under our core product strategy, we expect to progress five RNAi therapeutic programs into advanced stages of clinical development by the end of 2015. While focusing our efforts on our core product strategy, we also intend to continue to advance additional partner-based development programs through existing or future alliances.

In addition, we continue to work internally and with third-party collaborators to develop new technologies to deliver our RNAi therapeutics both directly to specific sites of disease, and systemically by intravenous or subcutaneous administration.

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

- our ability to discover new product candidates;
- our ability to progress product candidates into pre-clinical and clinical trials;
- the scope, rate of progress and cost of our pre-clinical trials and other research and development activities, including those related to developing safe and effective ways of delivering siRNAs into cells and tissues;
- the scope, rate of progress and cost of any clinical trials we commence;
- clinical trial results;
- the cost of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the terms, timing and success of any collaboration, licensing and other arrangements that we may establish;
- the cost, timing and success of regulatory filings and approvals or potential changes in regulations that govern our industry or the way in which they are interpreted or enforced;
- the cost and timing of establishing sufficient sales, marketing and distribution capabilities;
- the cost and timing of establishing sufficient clinical and commercial supplies for any product candidates and products that we may develop;
- the costs associated with legal activities, including litigation, arising in the course of our business activities and our ability to prevail in any such legal disputes; 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 Part II, Item 1A below under the heading Risk Factors.

Table of Contents

Strategic Alliances

A significant component of our business plan is to enter into strategic alliances and collaborations with pharmaceutical and biotechnology companies, academic institutions, research foundations and others, as appropriate, to gain access to funding, capabilities, technical resources and intellectual property to further our development efforts and to generate revenues. We also seek to form or advance new ventures and opportunities in areas outside our primary focus on RNAi therapeutics.

To generate revenues from our intellectual property rights, we also grant licenses to biotechnology companies under our InterfeRx program for the development and commercialization of RNAi therapeutics for specified targets in which we have no direct strategic interest. We also license key aspects of our intellectual property to companies active in the research products and services market, which includes the manufacture and sale of reagents. Our InterfeRx and research product licenses aim to generate modest near-term revenues that we can re-invest in the development of our proprietary RNAi therapeutics pipeline. At June 30, 2011, we had granted such licenses, on both an exclusive and non-exclusive basis, to approximately 20 companies.

Since delivery of RNAi therapeutics remains a major objective of our research activities, we also look to form collaboration and licensing arrangements with other companies and academic institutions to gain access to delivery technologies. For example, we have entered into agreements with Tekmira Pharmaceuticals Corporation, or Tekmira, the Massachusetts Institute of Technology, or MIT, The University of British Columbia, or UBC, and AlCana Technologies, Inc., or AlCana, among others, to focus on various delivery strategies. We have also entered into license agreements with Isis, Max Planck Innovation GmbH (formerly known as Garching Innovation GmbH), or Max Planck Innovation, Tekmira, MIT, Cancer Research Technology Limited, or CRT, Whitehead Institute for Biomedical Research, or Whitehead, Stanford University, or Stanford, The University of Texas Southwestern Medical Center, or UTSW, as well as a number of other entities, to obtain rights to intellectual property in the field of RNAi.

Finally, we seek funding for the development of our proprietary RNAi therapeutics pipeline from the government and foundations. For example, in 2006, the NIAID awarded us a contract to advance the development of a broad spectrum RNAi anti-viral therapeutic against hemorrhagic fever virus, including the Ebola virus, which contract ended in December 2010.

UBC/AlCana Delivery Collaboration. Our research agreement with UBC and AlCana entered into in July 2009 is focused on the discovery of novel lipids, such as the MC3 lipid, employed in second-generation LNP formulations for the systemic delivery of RNAi therapeutics. Pursuant to the terms of the research agreement, we were funding collaborative research over an initial two-year period, and recently exercised our right to extend the collaborative research and our funding for a third year, through July 2012. The collaborative research is being conducted by our scientists, together with scientists at UBC and AlCana.

Under the research agreement, we have exclusive rights to all new inventions relating to the delivery of oligonucleotides and other nucleic acid constructs, as well as sole rights to sublicense any resulting intellectual property to our current and future collaborators. UBC and AlCana are eligible to receive up to an aggregate of $1.3 million in milestone payments from us for each licensed product (as defined in the research agreement) directed to a particular target (as defined in the research agreement), together with single-digit royalty payments on annual product sales.

Concurrent with the execution of the research agreement, we also entered into a supplemental agreement with Tekmira, Protiva Biotherapeutics Inc., a wholly-owned subsidiary of Tekmira, or Protiva, UBC and AlCana, which contains additional terms regarding the intellectual property rights arising out of the research agreement. Pursuant to the terms of the supplemental agreement, each of Tekmira and Protiva has the right to use new inventions under the research agreement for its own RNAi therapeutic programs that are licensed under our InterfeRx program and would be required to pay milestones and royalties to UBC and AlCana in connection with such use.

Pursuant to the terms of the supplemental agreement, each of Tekmira and Protiva waived all prohibitions and restrictions on certain former Tekmira employees who are now working at UBC and AlCana in connection with their performance of the collaborative research under the research agreement and granted us, AlCana, UBC and such former Tekmira employees a covenant not to sue for any cause of action relating to such activities that arose out of their former employment with Tekmira.

The subject matter of these agreements is the subject of ongoing litigation between Tekmira and Protiva, on the one hand, and us and AlCana, on the other hand, a description of which is set forth below under Part II, Item 1 Legal Proceedings.

Takeda Alliance. Under our collaboration agreement with Takeda, Takeda agreed to pay us $50.0 million upon achievement of specified technology transfer milestones. Of this $50.0 million, $20.0 million was paid to us in October 2008, $20.0 million was paid to us in March 2010 and the final $10.0 million was paid to us in March 2011.

Table of Contents

Alnylam Biotherapeutics

Since 2009, we have advanced our efforts regarding the application of RNAi technologies to improve the manufacturing processes for biologics, including recombinant proteins and monoclonal antibodies. These applications of RNAi technology, which we are advancing in an internal effort referred to as Alnylam Biotherapeutics, have the potential to create new business opportunities. In particular, we are advancing RNAi technologies to improve the quantity and quality of biologics manufacturing processes using mammalian cell culture, such as Chinese hamster ovary, or CHO, cells. This RNAi technology potentially could be applied to the improvement of manufacturing processes for existing marketed drugs, new drugs in development and for the emerging biosimilars market. We have developed proprietary delivery lipids that enable the efficient delivery of siRNAs into CHO cells when grown in suspension culture, as well as other cell systems that are used for the manufacture of biologics. Studies have demonstrated that silencing certain target genes involved in certain CHO cell apoptotic and metabolic pathways resulted in improved cell viability as compared with untreated cells. Additional studies demonstrated the ability to target a viral infection of CHO cells and alter glycosylation pathways. During 2010, Alnylam Biotherapeutics formed two collaborations with leading biotechnology and pharmaceutical companies. As Alnylam Biotherapeutics advances the technology, it plans to seek additional collaborations with established biologic manufacturers, selling licenses, products and services.

microRNA Therapeutics

Regulus. In September 2007, we and Isis established Regulus, a company focused on the discovery, development and commercialization of microRNA therapeutics. Regulus leverages our and Isis technologies, know-how and intellectual property relating to microRNA therapeutics.

Regulus, which initially was established as a limited liability company, converted to a C corporation as of January 2, 2009 and changed its name to Regulus Therapeutics Inc. In consideration for our and Isis initial interests in Regulus, we and Isis each granted Regulus exclusive licenses to our intellectual property for certain microRNA therapeutics as well as certain patents in the microRNA field. At June 30, 2011, we, Isis and Sanofi owned approximately 45%, 46% and 9%, respectively, of Regulus. Regulus continues to operate as an independent company with a separate board of directors, scientific advisory board and management team, some of whom have options to purchase common stock of Regulus.

Regulus is exploring therapeutic opportunities that arise from microRNA dysregulation. Since microRNAs are believed to regulate broad networks of genes and biological pathways, microRNA therapeutics define a new and potentially high-impact strategy to target multiple nodes on disease pathways. microRNAs are small non-coding RNAs that regulate the expression of other genes. There are approximately 700 microRNAs that have been identified in the human genome, and these are believed to regulate the expression of up to 30% of all human genes. Since microRNAs may act as master regulators of the genome and are often found to be dysregulated in disease, microRNAs potentially represent an exciting new platform for drug discovery and development. Regulus is advancing microRNA therapeutics in several areas including fibrosis, hepatitis C virus, or HCV, infection, immuno-inflammatory diseases, metabolic and cardiovascular diseases, and oncology.

In April 2008, Regulus entered into a worldwide strategic alliance with GSK to discover, develop and market novel microRNA-targeted therapeutics to treat inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. In connection with this alliance, Regulus received $20.0 million in upfront payments from GSK, including a $15.0 million option fee and a loan of $5.0 million (guaranteed by us and Isis) that will convert into Regulus common stock under certain specified circumstances. Regulus is eligible to receive development, regulatory and sales milestone payments for each of the four microRNA-targeted therapeutics discovered and developed as part of the alliance, and would also receive royalty payments on worldwide sales of products resulting from the alliance, if any. In May 2009, Regulus achieved the first demonstration of a pharmacological effect in immune cells by specific microRNA inhibition, the initial discovery milestone under the GSK alliance, which triggered a payment under the agreement. In July 2011, Regulus and GSK identified a third microRNA target under this alliance triggering an additional pre-clinical milestone payment from GSK.

In February 2010, Regulus and GSK established a new collaboration to develop and commercialize microRNA therapeutics targeting miR-122 in all fields, with the treatment of HCV infection as the lead indication. Under the

terms of this collaboration, Regulus received $8.0 million in upfront payments from GSK, including a $3.0 million license fee and a loan of $5.0 million (guaranteed by us and Isis) that will convert into Regulus common stock under certain specified circumstances. Consistent with the original GSK alliance, Regulus is eligible to receive development, regulatory and sales milestone payments, as well as royalty payments on worldwide sales of products resulting from the alliance, if any, as Regulus and GSK advance microRNA therapeutics targeting miR-122.

Table of Contents

In June 2010, Regulus entered into a global, strategic alliance with Sanofi to discover, develop and commercialize microRNA therapeutics on up to four microRNA targets. Under the terms of this alliance, Regulus received $25.0 million in upfront fees and is entitled to annual research support for three years with the option to extend research support for two additional years. In addition, Regulus is eligible to receive royalties on microRNA therapeutic products commercialized by Sanofi, if any. Sanofi will support 100% of the costs of clinical development and commercialization of each program. The alliance will initially focus on the therapeutic area of fibrosis. Regulus and Sanofi will collaborate on up to four microRNA targets, including Regulus lead fibrosis program targeting miR-21. Sanofi also received an option for a broader technology alliance with Regulus that provides Regulus certain rights to participate in development and commercialization of resulting products. If exercised, this option is worth up to an additional $50.0 million to Regulus. We and Isis are each eligible to receive 7.5% of all potential upfront and milestone payments, in addition to single-digit royalties on product sales, if any. We received $1.9 million from Regulus in connection with this alliance, representing 7.5% of the $25.0 million upfront payment from Sanofi to Regulus. In addition, in October 2010, Sanofi made a $10.0 million equity investment in Regulus.

Intellectual Property

The strength of our intellectual property portfolio relating to the development and commercialization of siRNAs as therapeutics is essential to our business strategy. We own or license issued patents and pending patent applications in the United States and in key markets around the world claiming fundamental features of siRNAs and RNAi therapeutics as well as those claiming crucial chemical modifications and promising delivery technologies. Specifically, we have a portfolio of patents, patent applications and other intellectual property covering: fundamental aspects of the structure and uses of siRNAs, including their use as therapeutics, and RNAi-related mechanisms; chemical modifications to siRNAs that improve their suitability for therapeutic uses; siRNAs directed to specific targets as treatments for particular diseases; delivery technologies, such as in the field of cationic liposomes; and all aspects of our specific development candidates.

We believe that no other company possesses a portfolio of such broad and exclusive rights to the patents and patent applications required for the commercialization of RNAi therapeutics. Our intellectual property estate for RNAi therapeutics includes over 1,800 active cases and over 700 granted or issued patents, of which over 300 are issued or granted in the United States, the European Union and Japan. We continue to seek to grow our portfolio through the creation of new technology in this field. In addition, we are very active in our evaluation of third-party technologies.

Our expertise in RNAi therapeutics and broad intellectual property estate have allowed us to form alliances with leading companies, including Isis, Medtronic, Novartis, Biogen, Roche, Takeda, Kyowa Hakko Kirin and Cubist, as well as license agreements with other biotechnology companies interested in developing RNAi therapeutic products and research companies that commercialize RNAi reagents or services.

Given the importance of our intellectual property portfolio to our business operations, we intend to vigorously enforce our rights and defend against challenges that have arisen or may arise in this area.

Critical Accounting Policies and Estimates

Revenue Recognition

In January 2011, we adopted new authoritative guidance on revenue recognition for multiple element arrangements. The guidance, which applies to multiple element arrangements entered into or materially modified on or after January 1, 2011, amends the criteria for separating and allocating consideration in a multiple element arrangement by modifying the fair value requirements for revenue recognition and eliminating the use of the residual method. The fair value of deliverables under the arrangement may be derived using a best estimate of selling price if vendor specific objective evidence and third-party evidence is not available. Deliverables under the arrangement will be separate units of accounting provided (i) a delivered item has value to the customer on a standalone basis; and (ii) if the arrangement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the control of the vendor. We did not enter into any significant multiple element arrangements or materially modify any of our existing multiple element arrangements during the six months ended June 30, 2011. Our existing license and collaboration agreements continue to be accounted for under previously issued revenue recognition guidance for multiple element arrangements.

Table of Contents

Except as noted above, there have been no significant changes to our critical accounting policies since the beginning of this fiscal year. Our other critical accounting policies are described in the Management s 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, 2010, which we filed with the SEC on February 18, 2011.

Results of Operations

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2011	2010	2011	2010
Net revenues	$ 20,614	$ 26,617	$ 41,511	$ 51,181
Operating expenses	33,732	38,243	70,305	74,113
Loss from operations	(13,118)	(11,626)	(28,794)	(22,932)
Net loss	$ (13,824)	$ (14,632)	$ (30,109)	$ (26,955)

Net Revenues from Research Collaborators

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2011	2010	2011	2010
Roche	$ 13,994	$ 13,994	$ 27,988	$ 27,988
Takeda	5,493	5,489	11,261	10,923
Novartis	59	2,614	118	4,973
Government contract	44	1,521	150	3,087
Other research collaborator	822	2,696	1,643	3,517
InterfeRx program, research reagent license and other	202	303	351	693
Total net revenues from research collaborators	$ 20,614	$ 26,617	$ 41,511	$ 51,181

The decrease in Novartis revenues for the three and six months ended June 30, 2011 as compared to the three and six months ended June 30, 2010 was due primarily to the planned completion of the fifth and final year of the research program under the Novartis collaboration and license agreement in October 2010. The decrease in government contract revenues for the three and six months ended June 30, 2011 as compared to the three and six months ended June 30, 2010 was primarily a result of the completion of our contract with the NIAID in December 2010. The decrease in other research collaborator revenues was primarily as a result of the $1.9 million sublicense fee recognized in connection with Regulus June 2010 alliance with Sanofi, representing 7.5% of the $25.0 million upfront payment from Sanofi to Regulus.

Table of Contents

Total deferred revenue of $180.8 million at June 30, 2011 consists of payments we have received from collaborators, primarily Roche, Takeda, Kyowa Hakko Kirin and Cubist, but have not yet recognized pursuant to our revenue recognition policies.

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

Operating expenses

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

	Three Months Ended June 30, 2011	% of Total Operating Expenses	Three Months Ended June 30, 2010	% of Total Operating Expenses	Decrease $	Decrease %
Research and development	$ 25,303	75%	$ 28,136	74%	$ (2,833)	(10)%
General and administrative	8,429	25%	10,107	26%	(1,678)	(17)%
Total operating expenses	$ 33,732	100%	$ 38,243	100%	$ (4,511)	(12)%

	Six Months Ended June 30, 2011	% of Total Operating Expenses	Six Months Ended June 30, 2010	% of Total Operating Expenses	Decrease $	Decrease %
Research and development	$ 51,652	73%	$ 52,836	71%	$ (1,184)	(2)%
General and administrative	18,653	27%	21,277	29%	(2,624)	(12)%
Total operating expenses	$ 70,305	100%	$ 74,113	100%	$ (3,808)	(5)%

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 June 30, 2011	% of Expense Category	Three Months Ended June 30, 2010	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
Research and development						
Clinical trial and manufacturing	$ 6,569	26%	$ 5,871	21%	$ 698	12%
Compensation and related	5,871	23%	6,268	22%	(397)	(6)%
External services	4,486	18%	5,908	21%	(1,422)	(24)%

Facilities-related	3,102	12%	3,044	11%	58	2%
Non-cash stock-based compensation	2,830	11%	3,246	12%	(416)	(13)%
Lab supplies and materials	1,594	6%	2,118	8%	(524)	(25)%
License fees	43	*%	718	2%	(675)	(94)%
Other	808	4%	963	3%	(155)	(16)%
Total research and development expenses	$ 25,303	100%	$ 28,136	100%	$ (2,833)	(10)%

* Indicates less than 1%

Research and development expenses decreased during the three months ended June 30, 2011 as compared to the three months ended June 30, 2010 due primarily to lower external service expenses, including pre-clinical costs associated with our ALN-TTR and ALN-VSP programs. License fees decreased during the three months ended June 30, 2011 as compared to the three months ended June 30, 2010 as a result of license agreements entered into during the three months ended June 30, 2010. Lab supplies and materials and compensation and related expenses also decreased during the three months ended June 30, 2011 as compared to the three months ended June 30, 2010 due primarily to the reduction in workforce in connection with our September 2010 corporate restructuring. Partially offsetting these decreases was an increase in clinical trial and manufacturing expenses as we continue to advance our clinical programs.

Table of Contents

We expect to continue to devote a substantial portion of our resources to research and development expenses as we continue development of our and our collaborators product candidates and focus on continuing to develop drug delivery-related technologies, however, we expect that research and development expenses will remain consistent in the second half of 2011.

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

	Six Months Ended June 30, 2011	% of Expense Category	Six Months Ended June 30, 2010	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
Research and development						
Clinical trial and manufacturing	$ 12,760	25%	$ 10,275	20%	$ 2,485	24%
Compensation and related	12,203	24%	12,318	23%	(115)	(1)%
External services	9,420	18%	10,487	20%	(1,067)	(10)%
Facilities-related	6,463	12%	5,918	11%	545	9%
Non-cash stock-based compensation	5,495	11%	6,475	12%	(980)	(15)%
Lab supplies and materials	3,276	6%	4,268	8%	(992)	(23)%
License fees	349	1%	1,181	2%	(832)	(70)%
Other	1,686	3%	1,914	4%	(228)	(12)%
Total research and development expenses	$ 51,652	100%	$ 52,836	100%	$ (1,184)	(2)%

Research and development expenses decreased during the six months ended June 30, 2011 as compared to the six months ended June 30, 2010 due primarily to lower external service expenses, including pre-clinical costs associated with our ALN-TTR and ALN-VSP programs. Partially offsetting this decrease was an increase in clinical trial and manufacturing expenses as we continue to advance our clinical programs.

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

	Three Months Ended June 30, 2011	% of Expense Category	Three Months Ended June 30, 2010	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
General and administrative						

Consulting and professional services	$ 4,198	50%	$ 5,499	54%	$ (1,301)	(24)%
Compensation and related	1,707	20%	1,575	16%	132	8%
Non-cash stock-based compensation	1,384	16%	1,822	18%	(438)	(24)%
Facilities-related	591	7%	583	6%	8	1%
Other	549	7%	628	6%	(79)	(13)%
Total general and administrative expenses	$ 8,429	100%	$ 10,107	100%	$ (1,678)	(17)%

The decrease in general and administrative expenses during the three months ended June 30, 2011 as compared to the three months ended June 30, 2010 was due primarily to lower consulting and professional services expenses related to business activities, primarily legal activities, a description of which is set forth below under Part II, Item 1 Legal Proceedings.

We expect that general and administrative expenses will remain consistent in the second half of 2011.

Table of Contents

	Six Months Ended June 30, 2011	% of Expense Category	Six Months Ended June 30, 2010	% of Expense Category	Increase (Decrease) $	Increase (Decrease) %
General and administrative						
Consulting and professional services	$ 9,674	52%	$ 11,635	55%	$ (1,961)	(17)%
Compensation and related	3,764	20%	3,225	15%	539	17%
Non-cash stock-based compensation	2,841	15%	3,920	18%	(1,079)	(28)%
Facilities-related	1,258	7%	1,185	6%	73	6%
Other	1,116	6%	1,312	6%	(196)	(15)%
Total general and administrative expenses	$ 18,653	100%	$ 21,277	100%	$ (2,624)	(12)%

The decrease in general and administrative expenses during the six months ended June 30, 2011 as compared to the six months ended June 30, 2010 was due primarily to lower consulting and professional services expenses related to business activities, primarily legal activities, a description of which is set forth below under Part II, Item 1 Legal Proceedings.

Other income (expense)

We incurred $1.0 million and $2.1 million of equity in loss of joint venture (Regulus Therapeutics Inc.) for the three and six months ended June 30, 2011, respectively, as compared to $3.9 million and $5.5 million for the three and six months ended June 30, 2010, respectively, related to our share of the net losses incurred by Regulus.

Interest income was $0.3 million and $0.7 million for the three and six months ended June 30, 2011, respectively, as compared to $0.6 million and $1.2 million for the three and six months ended June 30, 2010, respectively. The decrease was due primarily to lower average cash, cash equivalent and marketable securities balances.

Liquidity and Capital Resources

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

	Six Months Ended June 30, 2011	2010
Net loss	$ (30,109)	$ (26,955)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities	13,320	18,187
Changes in operating assets and liabilities	(16,095)	(31,147)
Net cash used in operating activities	(32,884)	(39,915)
Net cash provided by (used in) investing activities	24,924	(34,425)
Net cash provided by financing activities	471	3,083
Effect of exchange rate on cash		(29)
Net decrease in cash and cash equivalents	(7,489)	(71,286)
Cash and cash equivalents, beginning of period	74,599	137,468

Cash and cash equivalents, end of period	$ 67,110	$ 66,182

Since we commenced operations in 2002, we have generated significant losses. At June 30, 2011, we had an accumulated deficit of $373.5 million. At June 30, 2011, we had cash, cash equivalents and marketable securities of $316.0 million, compared to cash, cash equivalents and marketable securities of $349.9 million at December 31, 2010. We invest primarily in cash equivalents, U.S. government and municipal obligations, high-grade corporate notes and commercial paper. Our investment objectives are, primarily, to assure liquidity and preservation of capital and, secondarily, to obtain investment income. All of our investments in debt securities are recorded at fair value and are available-for-sale. Fair value is determined based on quoted market prices and models using observable data inputs. We have not recorded any impairment charges related to our fixed income marketable securities at June 30, 2011.

Operating activities

We have required significant amounts of cash to fund our operating activities as a result of net losses since our inception.

Table of Contents

For the six months ended June 30, 2011, net cash used in operating activities of $32.9 million was due primarily to our net loss and a decrease in deferred revenue of $30.3 million. These amounts were partially offset by the receipt of our income tax refund of $10.7 million in March 2011. In addition, net cash used in operating activities is adjusted for non-cash items to reconcile net loss to net cash used in or provided by operating activities. These non-cash adjustments consist primarily of stock-based compensation, equity in loss of joint venture (Regulus Therapeutics Inc.), and depreciation and amortization.

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

Investing activities

For the six months ended June 30, 2011, net cash provided by investing activities of $24.9 million resulted primarily from net sales and maturities of marketable securities. For the six months ended June 30, 2010, net cash used in investing activities of $34.4 million resulted primarily from net purchases of marketable securities of $31.9 million and purchases of property and equipment of $2.5 million related to our Cambridge facility.

Financing activities

For the six months ended June 30, 2011, net cash of $0.5 million provided by financing activities was due to proceeds from the issuance of common stock in connection with stock option exercises. For the six months ended June 30, 2010, net cash provided by financing activities of $3.1 million was due to proceeds of $1.0 million from our issuance of common stock to Novartis in April 2010, as well as proceeds from the issuance of common stock in connection with stock option exercises.

Operating Capital Requirements

We do not know when, if ever, we will successfully develop or be able to commence sales of any product. Therefore, we anticipate that we will continue to generate significant losses for the foreseeable future as a result of planned expenditures for research and development activities relating to our drug development programs, including the development of drug delivery technologies and clinical trial costs, extension of the capabilities of our technology platform, including through business initiatives, continued management and growth of our patent portfolio, collaborations and general corporate activities. Based on our current operating plan, we believe that our existing cash, cash equivalents and fixed income marketable securities, for which we have not recognized any impairment charges, together with the cash we expect to generate under our current alliances, will be sufficient to fund our planned operations for at least the next several years, For this and other reasons discussed below, we may require significant additional funds earlier than we currently expect in order to develop, conduct clinical trials for and commercialize any product candidates.

In the future, we may seek additional funding through additional collaborative arrangements and public or private financings. In July 2011, we filed a shelf registration statement with the SEC for an indeterminate number of shares of common stock and/or other securities, for up to an aggregate of $150 million, for future issuance. During the current downturn in global financial markets, some companies have experienced difficulties accessing their cash equivalents and investment securities and raising capital generally, which have had a material adverse impact on their liquidity. The current economic downturn has diminished the availability of capital and may limit our ability to access these markets to obtain financing in the future. As a result of these and other factors, 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. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. If we are unable to obtain funding on a timely basis, we may be required to significantly delay or curtail one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue.

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

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

Table of Contents

our ability to develop relatively standard procedures for selecting and modifying siRNA product 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 or foundation contracts, if any;

our ability to maintain and establish additional collaborative arrangements and/or new business initiatives;

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

the resources, time and cost required for the preparation, filing, prosecution, maintenance and enforcement of patent claims;

our ability to successfully manage the potential impact of our corporate restructuring and workforce reduction on our culture, collaborative relationships and business operations;

the costs associated with legal activities, including litigation, arising in the course of our business activities and our ability to prevail in any such legal disputes;

progress in the research and development programs of Regulus; and

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

Contractual Obligations and Commitments

The disclosure of our contractual obligations and commitments is set forth under the heading Management s Discussion and Analysis of Financial Condition and Results of Operations Contractual Obligations and Commitments in our Annual Report on Form 10-K for the year ended December 31, 2010. There have been no material changes in our contractual obligations and commitments since December 31, 2010.

Recent Accounting Pronouncements

In May 2011, the Financial Accounting Standards Board, or FASB, issued a new accounting standard that clarifies the application of certain existing fair value measurement guidance and expands the disclosures for fair value measurements that are estimated using significant unobservable (Level 3) inputs. This new standard is effective on a prospective basis for annual and interim reporting periods beginning on or after December 15, 2011. We do not expect that adoption of this new standard will have a material impact on our condensed consolidated financial statements.

In June 2011, the FASB issued a new accounting standard that eliminates the option to present the components of other comprehensive income as part of the statement of changes in stockholders equity, requires the consecutive presentation of the statement of net income and other comprehensive income and requires an entity to present reclassification adjustments on the face of the financial statements from other comprehensive income to net income. The amendments in this new standard do not change the items that must be reported in other comprehensive income or when an item of other comprehensive income must be reclassified to net income nor do the amendments affect how earnings per share is calculated or presented. This new standard is required to be applied retrospectively and is effective for fiscal years and interim periods within those years beginning after December 15, 2011. As this new standard only requires enhanced disclosure, the adoption of this standard will not impact our condensed consolidated financial statements.

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 and municipal obligations, high-grade corporate notes and commercial paper. All of our investments in debt securities are classified as available-for-sale and are recorded at fair value. Our available-for-sale investments in debt securities are sensitive to changes in interest rates and changes in the credit ratings of the issuers. Interest rate changes would result in a change in the net fair value of these financial instruments due to the difference between the market interest rate and the market interest rate at the date of purchase of the financial instrument. If market interest rates were to increase immediately and uniformly by 50 basis points, or one-half of a percentage point, from levels at June 30, 2011, the net fair value of our interest-sensitive financial instruments would have resulted in a hypothetical decline of $1.1 million. A downgrade in the credit rating of an issuer of a debt security or further deterioration of the credit markets could result in a decline in the fair value of the debt instruments. Our investment guidelines prohibit investment in auction rate securities and we do not believe we have any direct exposure to losses relating from mortgage-based securities or derivatives related thereto such as credit-default swaps. We have not recorded any impairment charges to our fixed income marketable securities at June 30, 2011.

ITEM 4. CONTROLS AND PROCEDURES.

Our management, with the participation of our chief executive officer and vice president of finance and treasurer, evaluated the effectiveness of our disclosure controls and procedures as of June 30, 2011. The term disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means

Table of Contents

controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC s rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company s management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of June 30, 2011, 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 three months ended June 30, 2011 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS.

Tekmira Litigation

On March 16, 2011, Tekmira and Protiva filed a civil complaint in the Business Litigation Section of the Suffolk County Superior Court, in Boston, Massachusetts against us and on June 3, 2011, the plaintiffs filed an amended complaint adding AlCana, a research collaborator of ours, as a defendant. The amended complaint alleges misappropriation of the plaintiffs confidential and proprietary information and trade secrets, civil conspiracy, and tortious interference with contractual relationships by us and AlCana, and unjust enrichment, contractual breach, breach of the implied covenant of good faith and fair dealing, unfair competition, false advertising, and unfair and deceptive trade practices by us, and seeks injunctive relief and unspecified damages and other relief. On April 6, 2011, we timely served and filed an answer to the plaintiffs original complaint denying the plaintiffs claims in this action, together with counterclaims against the plaintiffs. On June 28, 2011, we timely served and filed an answer to the plaintiffs amended complaint denying the plaintiffs claims and counterclaims against the plaintiffs asserting breach of contract, defamation, breach of covenant not to sue, breach of patent prosecution and non-use provisions, misappropriation of confidential and proprietary information and trade secrets, unjust enrichment, breach of the implied covenant of good faith and fair dealing, as well as violations of Massachusetts statutes. We are seeking the dismissal of plaintiffs claims and judgment in our favor, as well as damages and equitable relief.

University of Utah Litigation

On March 22, 2011, The University of Utah, or the University, filed a civil complaint in the United States District Court for the District of Massachusetts by against us, Max Planck Gesellschaft Zur Forderung Der Wissenschaften E.V. and Max Planck Innovation, together, Max Planck, Whitehead, MIT and the University of Massachusetts, or UMass, claiming a professor at the University is the sole inventor, or in the alternative, a joint inventor, of the Tuschl patents. The University did not serve the original complaint on us or the other defendants. On July 6, 2011, the University filed an amended complaint alleging substantially the same claims against us, Max Planck, Whitehead, MIT and UMass. The amended complaint was served on us on July 14, 2011. The University is seeking changes to the inventorship of the Tuschl patents, unspecified damages and other relief.

Although we believe we have meritorious defenses to each of the claims in the lawsuits described above and intend to fully defend ourselves in these matters, litigation is subject to inherent uncertainty and a court could ultimately rule against us in one or both of these matters. In addition, the defense of litigation and related matters are costly and may divert the attention of our management and other resources that would otherwise be engaged in running our business.

Table of Contents

ITEM 1A. RISK FACTORS.

Our business is subject to numerous risks. We caution you that the following important factors, among others, could cause our actual results to differ materially from those expressed in forward-looking statements made by us or on our behalf in filings with the SEC, press releases, communications with investors and oral statements. All statements other than statements relating to historical matters should be considered forward-looking statements. When used in this report, the words believe, expect, anticipate, may, could, intend, will, plan, target, goal and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these words. 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 explicitly disclaim any obligation to update any forward-looking statements to reflect events or circumstances that arise after the date hereof. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC.

Risks Related to Our Business

Risks Related to Being an Early Stage Company

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

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

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

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

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

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

potential for RNAi therapeutics.

Table of Contents

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

We have experienced significant operating losses since our inception. At June 30, 2011, we had an accumulated deficit of $373.5 million. To date, we have not developed any products nor generated any revenues from the sale of products. Further, we do not expect to generate any such revenues in the foreseeable future. We expect to continue to incur annual net operating losses over the next several years and will require substantial resources over the next several years as we expand our efforts to discover, develop and commercialize RNAi therapeutics. We anticipate that the majority of any revenue we generate over the next several years will be from alliances with pharmaceutical and biotechnology companies or funding from contracts with the government or foundations, but cannot be certain that we will be able to secure or maintain these alliances or contracts, or meet the obligations or achieve any milestones that we may be required to meet or achieve to receive payments. We anticipate that revenue derived from such sources will not be sufficient to make us consistently profitable.

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

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

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

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

- our progress in demonstrating that siRNAs can be active as drugs;
- our ability to develop relatively standard procedures for selecting and modifying siRNA product 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 or foundation contracts, if any;

our ability to maintain and establish additional collaborative arrangements and/or new business initiatives;

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

the resources, time and cost required for the preparation, filing, prosecution, maintenance and enforcement of patent claims;

our ability to successfully manage the potential impact of our corporate restructuring and workforce reduction on our culture, collaborative relationships and business operations;

the costs associated with legal activities, including litigation, arising in the course of our business activities and our ability to prevail in any such legal disputes;

progress in the research and development programs of Regulus; 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.

Even if our estimates are correct, 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, under our shelf registration statement or otherwise, further dilution to our stockholders will result. In addition, as a condition to providing additional funds to us, future investors may demand, and may be granted, rights superior to those of existing stockholders. Moreover, our investor rights agreement with Novartis provides Novartis with the right generally to maintain its ownership percentage in us, subject to certain exceptions. These rights continue until the earlier of any sale by Novartis of shares of our common stock and the expiration or termination of our license agreement with Novartis, subject to certain exceptions. Pursuant to the terms of its investor rights agreement with us, Novartis purchased an aggregate of 335,033 shares of our common stock, resulting in aggregate payments to us of $7.6 million. These purchases allowed Novartis to maintain its ownership position of approximately 13.4% of our outstanding common stock. While the exercise of these rights by Novartis has provided us with funding, and the exercise in the future by Novartis may provide us with additional funding under some circumstances, these exercises have caused, and any future exercise of these rights by Novartis 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 and, in the event of insolvency, would be paid before holders of equity securities received any distribution of corporate assets.

If we are unable to obtain funding on a timely basis, we may be required to significantly delay or curtail one or more of our research or development programs or undergo additional reductions in our workforce or other corporate restructuring activities. 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 condensed consolidated financial statements prove inaccurate, our actual results may vary from those reflected in our projections and accruals.

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

statements requires us to make estimates and judgments that affect the reported amounts of our assets, liabilities, revenues and expenses, the amounts of charges accrued by us and related disclosure of contingent assets and liabilities. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. We cannot assure you, however, that our estimates, or the assumptions underlying them, will be correct.

Table of Contents

The investment of our cash, cash equivalents and marketable securities is subject to risks which may cause losses and affect the liquidity of these investments.

At June 30, 2011, we had $316.0 million in cash, cash equivalents and marketable securities. We historically have invested these amounts in corporate bonds, commercial paper, securities issued by the U.S. government and municipal obligations, certificates of deposit and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. These investments are subject to general credit, liquidity, market and interest rate risks, including the impact of U.S. sub-prime mortgage defaults that have affected various sectors of the financial markets and caused credit and liquidity issues. We may realize losses in the fair value of these investments or a complete loss of these investments, which would have a negative effect on our condensed consolidated financial statements. In addition, should our investments cease paying or reduce the amount of interest paid to us, our interest income would suffer. These market risks associated with our investment portfolio may have an adverse effect on our results of operations, liquidity and financial condition.

Risks Related to Our Dependence on Third Parties

Our license and collaboration agreements with pharmaceutical companies are important to our business. If these pharmaceutical companies do not successfully develop drugs pursuant to these agreements or we develop drugs targeting the same diseases as our non-exclusive licensees, our business could be adversely affected.

In July 2007, we entered into a license and collaboration agreement with Roche. Under the license and collaboration agreement we granted Roche a non-exclusive license to our intellectual property to develop and commercialize therapeutic products that function through RNAi, subject to our existing contractual obligations to third parties. The license is limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases and may be expanded to include up to 18 additional therapeutic areas, comprising substantially all other fields of human disease, as identified and agreed upon by the parties, upon payment to us by Roche of an additional $50.0 million for each additional therapeutic area, if any. In addition, in exchange for our contributions under the collaboration agreement, for each RNAi therapeutic product developed by Roche, its affiliates, or sublicensees under the collaboration agreement, we are entitled to receive milestone payments upon achievement of specified development and sales events, totaling up to an aggregate of $100.0 million per therapeutic target, together with royalty payments based on worldwide annual net sales, if any. In November 2010, Roche announced the discontinuation of certain activities in research and early development, including their RNAi research efforts. Our license and collaboration agreement with Roche currently remains in effect. Roche may assign its rights and obligations under the license and collaboration agreement to a third party in connection with the sale or transfer of its entire RNAi business.

In May 2008, we entered into a similar license and collaboration agreement with Takeda, which is limited to the therapeutic areas of oncology and metabolic diseases, and which may be expanded to include up to 20 additional therapeutic areas, comprising substantially all other fields of human disease, as identified and agreed upon by the parties, upon payment to us by Takeda of an additional $50.0 million for each additional therapeutic area, if any. For each RNAi therapeutic product developed by Takeda, its affiliates and sublicensees, we are entitled to receive specified development and commercialization milestones, totaling up to $171.0 million per product, together with royalty payments based on worldwide annual net sales, if any. In addition, we agreed that we will not grant any other party rights to develop RNAi therapeutics in the Asian territory through May 2013.

In September 2010, Novartis exercised its right under our collaboration and license agreement to select 31 designated gene targets, for which Novartis has exclusive rights to discover, develop and commercialize RNAi therapeutic products using our intellectual property and technology. Under the terms of the collaboration and license agreement, for any RNAi therapeutic products Novartis develops against these targets, we are entitled to receive milestone payments upon achievement of certain specified development and annual net sales events, up to an aggregate of $75.0 million per therapeutic product, as well as royalties on annual net sales of any such product.

If Takeda, Novartis or, if Roche assigns our license, Roche s assignee, fails to successfully develop products using our technology, we may not receive any milestone or royalty payments under these agreements. In addition, even if Takeda is not successful in its efforts, we are limited in our ability to form alliances with other parties in the Asia territory until 2013. We also have the option under the Takeda agreement, exercisable until the start of Phase III

development, to opt-in under a 50-50 profit sharing agreement to the development and commercialization in the United States of up to four Takeda licensed products, and would be entitled to opt-in rights for two additional products for each additional field expansion, if any, elected by Takeda under the collaboration agreement. If Takeda fails to successfully develop products, we may not realize any economic benefit from these opt-in rights.

Table of Contents

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

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

We do not have any capability for sales, marketing or distribution and have limited capabilities for drug development. In addition, we believe that other companies are expending substantial resources in developing safe and effective means of delivering siRNAs to relevant cell and tissue types. Accordingly, we have entered into alliances with other companies and collaborators that we believe can provide such capabilities, and we intend to enter into additional alliances in the future. For example, we intend to enter into (1) non-exclusive platform and/or multi-target discovery alliances which will enable our collaborators to develop RNAi therapeutics and will bring in additional funding with which we can develop our RNAi therapeutics, and (2) worldwide or specific geographic partnerships on select RNAi therapeutic programs. In such alliances, we expect our current, and may expect our future, collaborators to provide substantial capabilities in delivery of RNAi therapeutics to the relevant cell or tissue type, clinical development, regulatory affairs, and/or marketing, sales and distribution. For example, under our agreements with MIT, Tekmira, UBC and AlCana, among others, we have access to certain existing delivery technologies and/or are developing additional delivery capabilities. In addition, under our collaboration with Medtronic, we are jointly developing ALN-HTT, an RNAi therapeutic for HD, which would be delivered using an implanted infusion device developed by Medtronic. The success of this collaboration will depend, in part, on Medtronic s expertise in the area of delivery of drugs by infusion device, something that they have never done before with our product candidates. In other alliances, we may expect our collaborators to develop, market and sell certain of our product candidates. We may have limited or no control over the development, sales, marketing and distribution activities of these third parties. Our future revenues may depend heavily on the success of the efforts of these third parties. For example, we will rely entirely on Kyowa Hakko Kirin for development and commercialization of any RNAi products for the treatment of RSV in Asia. If Kyowa Hakko Kirin is not successful in its commercialization efforts, our future revenues from RNAi therapeutics for the treatment of RSV may be adversely affected.

We may not be successful in entering into such alliances on favorable terms due to various factors, including our ability to successfully demonstrate proof of concept for our technology in man, our ability to demonstrate the safety and efficacy of our specific drug candidates, and the strength of our intellectual property. Even if we do succeed in securing any such alliances, we may not be able to maintain them if, for example, development or approval of a product 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 product 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 product 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 Takeda, Cubist and Medtronic. 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 product candidate, we may not have sufficient funds to develop that or any other product candidate internally, or to bring any product candidates to market. If we do not have sufficient funds to develop and bring our product candidates to market, we will not be able to generate sales revenues from these product 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 product candidates could be delayed or terminated.

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

Our current collaborations allow, and we expect that any future collaborations will allow, either party to terminate the

Table of Contents

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

In addition, if we have a dispute with a collaborator over the ownership of technology or other matters, or if a collaborator terminates its collaboration with us, for breach or otherwise, or determines not to pursue the research and development of RNAi therapeutics, it would be difficult for us to attract new collaborators and could adversely affect how we are perceived in the business and financial communities. Moreover, a collaborator, or in the event of a change in control of a collaborator or the assignment of a collaboration agreement to a third party, the successor entity or assignee, could determine that it is in its financial interest to:

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

- pursue higher-priority programs or change the focus of its development programs, which could affect the collaborator s commitment to us; or

- if it has marketing rights, choose to devote fewer resources to the marketing of our product candidates, if any are approved for marketing, than it does for product candidates developed without us.

If any of these occur, the development and commercialization of one or more product 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.

Regulus is important to our business. If Regulus does not successfully develop drugs pursuant to our license and collaboration agreement, our business could be adversely affected. In addition, disagreements between us and Isis regarding the development of microRNA technology may cause significant delays and other impediments in the development of this technology, which could negatively affect the value of the technology and our investment in Regulus.

In September 2007, we and Isis formed Regulus, of which we owned approximately 45% at June 30, 2011, to discover, develop and commercialize microRNA therapeutics. Regulus is exploring therapeutic opportunities that arise from dysregulation of microRNAs. Neither Regulus nor any other company has received regulatory approval to market therapeutics utilizing microRNA technology. In connection with the establishment of Regulus, we exclusively licensed to Regulus our intellectual property rights covering microRNA technology. Generally, we do not have rights to pursue microRNA therapeutics independently of Regulus. If Regulus is unable to discover, develop and commercialize microRNA therapeutics, our business could be adversely affected.

Moreover, Regulus has formed a collaboration with GSK pursuant to which GSK has provided Regulus with loans totaling $5.4 million, including accrued interest. These loans are guaranteed by us and Isis. If Regulus is unable to repay GSK or convert the loans into Regulus common stock, we could be liable for our share of these obligations, and our business could be adversely affected.

In addition, Regulus operates as an independent company, governed by a board of directors. We and Isis each can elect an equal number of directors to serve on the Regulus board. Regulus researches and develops microRNA projects and programs pursuant to an operating plan that is approved by its board. Any disagreements between Isis and us regarding a development decision or any other decision submitted to Regulus board may cause significant delays in the development and commercialization of microRNA technology and could negatively affect the value of our investment in Regulus.

We rely on third parties to conduct our clinical trials, and if they fail to fulfill their obligations, our development plans may be adversely affected.

We rely on independent clinical investigators, contract research organizations and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our clinical trials. We have and we plan to continue to contract with certain

Table of Contents

third-parties to provide certain services, including site selection, enrollment, monitoring and data management services. Although we depend heavily on these parties, we do not control them and therefore, we cannot be assured that these third-parties will adequately perform all of their contractual obligations to us. If our third-party service providers cannot adequately fulfill their obligations to us on a timely and satisfactory basis or if the quality and accuracy of our clinical trial data is compromised due to failure to adhere to our protocols or regulatory requirements or if such third-parties otherwise fail to meet deadlines, our development plans may be delayed or terminated.

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-current good manufacturing practice, or cGMP material for use in *in vitro* and *in vivo* experiments. Some of our product candidates utilize specialized formulations, such as liposomes or LNPs, whose scale-up and manufacturing could be very difficult. We also have very limited experience in such scale-up and manufacturing, requiring us to depend on a limited number of third parties, who might not be able to deliver in a timely manner, or at all. In order to develop products, apply for regulatory approvals and commercialize our products, we will need to develop, contract for, or otherwise arrange for the necessary manufacturing capabilities. We may manufacture clinical trial materials ourselves or we may rely on others to manufacture the materials we will require for any clinical trials that we initiate. There are a limited number of manufacturers that supply synthetic siRNAs. We currently rely on several contract manufacturers for our supply of synthetic siRNAs. There are risks inherent in pharmaceutical manufacturing that could affect the ability of our contract manufacturers to meet our delivery time requirements or provide adequate amounts of material to meet our needs. Included in these risks are synthesis and purification failures and contamination during the manufacturing process, which could result in unusable product and cause delays in our development process, as well as additional expense to us. To fulfill our siRNA requirements, we may also need to secure alternative suppliers of synthetic siRNAs. In addition to the manufacture of the synthetic siRNAs, we may have additional manufacturing requirements related to the technology required to deliver the siRNA to the relevant cell or tissue type. In some cases, the delivery technology we utilize is highly specialized or proprietary, and for technical and legal reasons, we may have access to only one or a limited number of potential manufacturers for such delivery technology. For example, under our agreements with Tekmira, we are obligated, subject to certain exceptions specified in our contract with Tekmira, to utilize Tekmira for the manufacture of all LNP-formulated product candidates covered by Tekmira s intellectual property beginning during pre-clinical development and continuing through Phase II clinical trials. Failure by manufacturers to properly formulate our siRNAs for delivery could result in unusable product. Furthermore, a breach by such manufacturers of their contractual obligations would cause delays in our discovery and development process, as well as additional expense to us.

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

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

- we may not be able to initiate or continue clinical trials of products that are under development;
- we may be delayed in submitting regulatory applications, or receiving regulatory approvals, for our product candidates;

we may lose the cooperation of our collaborators;

our products could be the subject of inspections by regulatory authorities;

we may be required to cease distribution or recall some or all batches of our products; and

Table of Contents

ultimately, we may not be able to meet commercial demands for our products.

If any 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 on reasonable terms, if at all. In some cases, the technical skills required to manufacture our product may be unique to the original manufacturer and we may have difficulty transferring such skills to a back-up or alternate supplier, or we may be unable to transfer such skills at all. In addition, if we are required to change manufacturers for any reason, we will be required to verify that the new manufacturer maintains facilities and procedures that comply with quality standards and with all applicable regulations and guidelines. The delays associated with the verification of a new manufacturer could negatively affect our ability to develop product candidates in a timely manner or within budget. Furthermore, a manufacturer may possess technology related to the manufacture of our product candidate that such manufacturer owns independently. This would increase our reliance on such manufacturer or require us to obtain a license from such manufacturer in order to have another third party manufacture our products.

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

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

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

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

our direct sales and marketing efforts may not be successful.

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

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

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

Risks Related to Managing Our Operations

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

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

We face intense competition for qualified individuals from numerous pharmaceutical and biotechnology companies, universities, governmental entities and other research institutions, many of which have substantially greater resources with which to reward qualified individuals than we do. In addition, as a result of our September 2010 corporate restructuring and workforce reduction, we may face additional challenges in retaining our existing employees and recruiting new employees to join our company as our business needs change. 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 future business plan.

Table of Contents

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

Since we commenced operations in 2002, we have grown substantially. At June 30, 2011, we had 173 employees in our facility in Cambridge, Massachusetts. We expect that as we seek to increase the number of product candidates we are developing we will need to expand our operations in the future. This growth may place a strain on our administrative and operational infrastructure. If product 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 due to our development progress, we expect that we will need to manage additional relationships with various collaborators, suppliers and other organizations. Our ability to manage our operations and future growth will require us to continue to improve our operational, financial and management controls, reporting systems and procedures. We may not be able to implement improvements to our management information and control systems in an efficient or timely manner and may discover deficiencies in existing systems and controls.

Our business and operations could suffer in the event of system failures.

Despite the implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war, and telecommunication and electrical failures. Such events could cause interruption of our operations. For example, the loss of pre-clinical trial data or data from completed or ongoing clinical trials for our product candidates could result in delays in our regulatory filings and development efforts and significantly increase our costs. To the extent that any disruption or security breach were to result in a loss of or damage to our data, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the development of our product candidates could be delayed.

Risks Related to Our Industry

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

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

Before obtaining regulatory approval for the commercial distribution of our product 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 product 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, and the historical failure rate for product candidates is high. We currently have several programs in clinical development. We are developing ALN-RSV01 for the treatment of RSV infection. In January 2008, we completed our GEMINI study, a Phase II clinical trial designed to evaluate the safety, tolerability and anti-viral activity of ALN-RSV01 in adult subjects experimentally infected with RSV. During 2009, we completed a Phase IIa clinical trial assessing the safety and tolerability of ALN-RSV01 in adult lung transplant patients naturally infected with RSV. In February 2010, we initiated a Phase IIb clinical trial to evaluate the clinical efficacy endpoints as well as safety of aerosolized ALN-RSV01 in adult lung transplant patients naturally infected with RSV. The objective of this Phase IIb clinical trial is to repeat and extend the clinical results observed in the Phase IIa clinical trial. In addition, in March 2009, we initiated a Phase I clinical trial of ALN-VSP, our first systemically delivered RNAi therapeutic. We are developing ALN-VSP for the treatment of primary and secondary liver cancer. In July 2010, we also initiated a Phase I clinical trial for ALN-TTR01, our second systemically delivered RNAi therapeutic, which targets the TTR gene for the treatment of ATTR. In July 2011, we filed a CTA with the MHRA to initiate a Phase I clinical trial of ALN-PCS for the treatment of severe hypercholesteremia. However, we may not be able to further advance these or any other product candidate through clinical trials.

If we enter into clinical trials, the results from pre-clinical testing or early clinical trials of a product candidate may not predict the results that will be obtained in subsequent human clinical trials of that product candidate or any other product candidate. For example, ALN-RSV01 may not demonstrate the same results in the Phase IIb clinical trial as it did in our Phase IIa clinical trial. In addition, ALN-VSP, ALN-TTR01 and our other systemically delivered therapeutics, such as ALN-PCS, employ novel delivery formulations that have yet to be extensively evaluated in

human clinical trials and proven safe and effective. We, the FDA or other applicable regulatory authorities, or an institutional review board, or IRB, or similar foreign review board or committee, may suspend clinical trials of a product candidate at any time for various reasons, including if we or they believe the subjects or patients

Table of Contents

participating in such trials are being exposed to unacceptable health risks. Among other reasons, adverse side effects of a product 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 product candidate for any or all indications of use.

Clinical trials of a new product candidate require the enrollment of a sufficient number of patients, including patients who are suffering from the disease the product candidate is intended to treat and who meet other eligibility criteria. Rates of patient enrollment are affected by many factors, including the size of the patient population, the age and condition of the patients, the stage and severity of disease, the nature of the protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease, the seasonality of infections and the eligibility criteria for the clinical trial. In our ALN-VSP clinical trial, one patient with advanced pancreatic neuroendocrine cancer with extensive involvement of the liver developed hepatic failure five days following the second dose of ALN-VSP and subsequently died; this was deemed possibly related to the study drug. Six additional patients treated at the same dose did not exhibit any evidence of hepatotoxicity. As of March 2011, the ALN-VSP clinical trial had completed enrollment and a maximum tolerated dose was reached. In addition, our ALN-TTR01 trial targets a small population of patients suffering from ATTR. Delays or difficulties in patient enrollment or difficulties retaining trial participants can result in increased costs, longer development times or termination of a clinical trial.

Clinical trials also require the review and oversight of IRBs, which approve and continually review clinical investigations and protect the rights and welfare of human subjects. Inability to obtain or delay in obtaining IRB approval can prevent or delay the initiation and completion of clinical trials, and the FDA or foreign regulatory authorities 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 product candidates that we develop may encounter problems during clinical trials that will cause us, an IRB or regulatory authorities to delay, suspend or terminate these trials, or that will delay or confound 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 product candidate that is affected, or development of any of our other product candidates. We may also lose, or be unable to enter into, collaborative arrangements for the affected product candidate and for other product candidates we are developing.

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

- 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;

- delays in filing INDs or comparable foreign applications or delays or failure in obtaining the necessary approvals from regulators or IRBs in order to commence a clinical trial at a prospective trial site, or their suspension or termination of a clinical trial once commenced;

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

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

- delays in enrolling patients and volunteers into clinical trials, and variability in the number and types of patients and volunteers available for clinical trials;

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

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

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

Table of Contents

greater than anticipated clinical trial costs;

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

poor effectiveness of our product candidates during clinical trials;

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

failure of our third-party contractors or investigators to comply with regulatory requirements or otherwise meet their contractual obligations in a timely manner, or at all;

governmental or regulatory delays and changes in regulatory requirements, policy and guidelines, including the imposition of additional regulatory oversight around clinical testing generally or with respect to our technology in particular; or

varying interpretations of data by the FDA and similar foreign regulatory agencies.

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

The regulatory approval process may be delayed for any products we develop that require the use of specialized drug delivery devices, which may require us to incur additional costs and delay receipt of any potential product revenue.

Some product candidates that we develop may need to be administered using specialized drug delivery devices that deliver RNAi therapeutics directly to diseased parts of the body. For example, we believe that product candidates we develop for 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 collaborations to develop alternative drug delivery systems, or utilize existing drug delivery systems, for the direct delivery of RNAi therapeutics for these diseases. While we expect to rely on drug delivery systems that have been approved by the FDA or other regulatory agencies to deliver drugs like ours to diseased parts of the body, 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 product candidate. In addition, the use of a specialized delivery system, even if previously approved, could complicate the design or analysis of clinical trials for our RNAi therapeutics. In summary, we may be unable to find, or experience delays in finding, suitable drug delivery systems to administer RNAi therapeutics directly to diseased parts of the body, which could negatively affect our ability to successfully commercialize these RNAi therapeutics.

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

Our product candidates are subject to extensive governmental regulations relating to, among other things, research, testing, development, manufacturing, safety, efficacy, approval, recordkeeping, reporting, labeling, storage, marketing and distribution of drugs. Rigorous pre-clinical testing and clinical trials and an extensive regulatory approval process are required to be successfully completed in the United States and in many foreign jurisdictions

before a new drug can be marketed. Satisfaction of these and other regulatory requirements is costly, time consuming, uncertain and subject to unanticipated delays. It is possible that none of the product candidates we may develop will obtain the regulatory approvals necessary for us or our collaborators to begin selling them.

We have very limited experience in conducting and managing the clinical trials necessary to obtain regulatory approvals, including approval by the FDA. The time required to obtain FDA and other approvals is unpredictable but typically takes many years

Table of Contents

following the commencement of clinical trials, depending upon the type, complexity and novelty of the product candidate. The standards that the FDA and its foreign counterparts use when regulating us are not always applied predictably or uniformly and can change. 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. It is impossible to predict whether legislative changes will be enacted, or whether FDA or foreign regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

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

Any delay or failure in obtaining required approvals could have a material adverse effect on our ability to generate revenues from the particular product candidate for which we are seeking approval. Furthermore, any regulatory approval to market a product may be subject to limitations on the approved uses for which we may market the product or the labeling or other restrictions. In addition, the FDA has the authority to require a Risk Evaluation and Mitigation Strategies, or REMS, plan as part of an NDA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug or biologic, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry. These limitations and restrictions may limit the size of the market for the product and affect reimbursement by third-party payors.

We are also subject to numerous foreign regulatory requirements governing, among other things, the conduct of clinical trials, manufacturing and marketing authorization, pricing and third-party reimbursement. The foreign regulatory approval process varies among countries and 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 ensure approval by regulatory authorities outside the United States and vice versa.

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 requirements, our approvals could be limited or withdrawn, we could be subject to other penalties, 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 surveillance to monitor the safety and efficacy of the drug product required as a condition of approval or agreed to by us. Any regulatory approvals that we receive for our product candidates may also be subject to limitations on the approved uses for which the product may be marketed. Other ongoing regulatory requirements include, among other things, submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMP requirements and good clinical practices for any clinical trials that we conduct post-approval. In addition, we are conducting, and intend to continue to conduct, clinical trials for our product candidates, and we intend to seek approval to market our product candidates, in jurisdictions outside of the United States, and therefore will be subject

to, and must comply with, regulatory requirements in those jurisdictions.

The FDA has significant post-market authority, including, for example, the authority to require labeling changes based on new safety information and to require post-market studies or clinical trials to evaluate serious safety risks related to the use of a drug and to require withdrawal of the product from the market. The FDA also has the authority to require a REMS plan after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug.

Table of Contents

The manufacturer and manufacturing facilities we use to make any of our product candidates will also be subject to periodic review and inspection by the FDA and other regulatory agencies. The discovery of any new or previously unknown problems with our third-party manufacturers, manufacturing processes or facilities, may result in restrictions on the drug or manufacturer or facility, including withdrawal of the drug from the market. We do not have, and currently do not intend to develop, the ability to manufacture material for our clinical trials or on a commercial scale. We may manufacture clinical trial materials or we may contract a third party to manufacture these materials for us. Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured products ourselves, including reliance on the third-party manufacturer for regulatory compliance. Our product promotion and advertising is also subject to regulatory requirements and continuing regulatory review.

If we or our collaborators, manufacturers or service providers fail to comply with applicable continuing regulatory requirements in the United States or foreign jurisdictions in which we may seek to market our products, we or they may be subject to, among other things, fines, warning letters, holds on clinical trials, refusal by the FDA to approve pending applications or supplements to approved applications, suspension or withdrawal of regulatory approval, product recalls and seizures, refusal to permit the import or export of products, operating restrictions, injunction, civil penalties and criminal prosecution.

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

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

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

- the timing of our receipt of any marketing approvals, the terms of any approvals and the countries in which approvals are obtained;
- the safety and efficacy of our product candidates, as demonstrated in clinical trials;
- relative convenience and ease of administration of our product candidates;
- the willingness of patients to accept potentially new routes of administration;
- the success of our physician education programs;
- the availability of adequate government and third-party payor reimbursement;
- the pricing of our products, particularly as compared to alternative treatments; and
- availability of alternative effective treatments for the diseases that product candidates we develop are intended to treat and the relative risks, benefits and costs of the treatments.

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

As a manufacturer of pharmaceuticals, we are subject to federal, state, and foreign healthcare laws and regulations pertaining to fraud and abuse and patients rights. These laws and regulations include:

- the U.S. federal healthcare program anti-kickback law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual for a healthcare item or service, or the purchasing or ordering of an item or service, for which payment may be made under a federal healthcare program such as Medicare or Medicaid;

42

Table of Contents

the U.S. federal false claims law, which prohibits, among other things, individuals or entities from knowingly presenting or causing to be presented, claims for payment by government funded programs such as Medicare or Medicaid that are false or fraudulent, and which may apply to us by virtue of statements and representations made to customers or third parties;

the U.S. federal Health Insurance Portability and Accountability Act, or HIPAA, and Health Information Technology for Economic and Clinical Health, or HITECH, Act, which prohibit executing a scheme to defraud healthcare programs; impose requirements relating to the privacy, security, and transmission of individually identifiable health information; and require notification to affected individuals and regulatory authorities of certain breaches of security of individually identifiable health information; and

state laws comparable to each of the above federal laws, such as, for example, anti-kickback and false claims laws applicable to commercial insurers and other non-federal payors, requirements for mandatory corporate regulatory compliance programs, and laws relating to patient data privacy and security.

If our operations are found to be in violation of any such requirements, we may be subject to penalties, including civil or criminal penalties, monetary damages, the curtailment or restructuring of our operations, loss of eligibility to obtain approvals from the FDA, or exclusion from participation in government contracting or other government programs, including Medicare and Medicaid, any of which could adversely our financial results. Although effective compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, these risks cannot be entirely eliminated. Any action against us for an alleged or suspected violation could cause us to incur significant legal expenses and could divert our management s attention from the operation of our business, even if our defense is successful. In addition, achieving and sustaining compliance with applicable laws and regulations may be costly to us in terms of money, time and resources.

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

adverse regulatory inspection findings;

warning letters;

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

restrictions on, or prohibitions against, marketing our products;

restrictions on, or prohibitions against, importation or exportation of our products;

suspension of review or refusal to approve pending applications or supplements to approved applications;

exclusion from participation in government-funded healthcare programs;

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

suspension or withdrawal of product approvals;

product seizures;

injunctions; and

civil and criminal penalties and fines.

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

Table of Contents

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

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

We currently expect that any drugs we develop may need to be administered under the supervision of a physician. Under currently applicable U.S. 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 standards 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 healthcare 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 and for which we obtain regulatory approval could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products, and our overall financial condition.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare and legislative and regulatory proposals to broaden the availability of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory changes in the healthcare system in the United States and other major healthcare markets have been proposed in recent years, and such efforts have expanded substantially in recent years. These developments have included prescription

drug benefit legislation that was enacted and took effect in January 2006, healthcare reform legislation enacted by certain states, and major healthcare reform legislation that was passed by Congress and enacted into law in the United States in 2010. These developments could, directly or indirectly, affect our ability to sell our products, if approved, at a favorable price.

In particular, in March 2010, the Patient Protection and Affordable Care Act, or PPACA, and a related reconciliation bill were signed into law. This new legislation changes the current system of healthcare insurance and benefits intended to broaden

Table of Contents

coverage and control costs. The new law also contains provisions that will affect companies in the pharmaceutical industry and other healthcare related industries by imposing additional costs and changes to business practices. Provisions affecting pharmaceutical companies include the following:

Mandatory rebates for drugs sold into the Medicaid program have been increased, and the rebate requirement has been extended to drugs used in risk-based Medicaid managed care plans.

The 340B Drug Pricing Program under the Public Health Services Act has been extended to require mandatory discounts for drug products sold to certain critical access hospitals, cancer hospitals and other covered entities.

Pharmaceutical companies are required to offer discounts on brand-name drugs to patients who fall within the Medicare Part D coverage gap, commonly referred to as the Donut Hole.

Pharmaceutical companies are required to pay an annual non-tax deductible fee to the federal government based on each company s market share of prior year total sales of branded products to certain federal healthcare programs, such as Medicare, Medicaid, Department of Veterans Affairs and Department of Defense. The aggregated industry-wide fee is expected to total $28 billion through 2019, of which $2.5 billion will be payable in 2011. Since we expect our branded pharmaceutical sales to constitute a small portion of the total federal health program pharmaceutical market, we do not expect this annual assessment to have a material impact on our financial condition.

The new law provides that biologic products may receive 12 years of market exclusivity, with a possible six-month extension for pediatric products. After this exclusivity ends, generic manufacturers will be permitted to enter the market, which is likely to reduce the pricing for such products and could affect the company s profitability. In addition, generic manufacturers will be permitted to challenge one or more of the patents for a branded drug after a product is marketed for four years.

The full effects of the U.S. healthcare reform legislation cannot be known until the new law is implemented through regulations or guidance issued by the Centers for Medicare & Medicaid Services and other federal and state healthcare agencies. The financial impact of the U.S. healthcare reform legislation over the next few years will depend on a number of factors, including but not limited, to the policies reflected in implementing regulations and guidance, and changes in sales volumes for products affected by the new system of rebates, discounts and fees. The new legislation may also have a positive impact on our future net sales, if any, by increasing the aggregate number of persons with healthcare coverage in the United States, but such increases are unlikely to be realized until approximately 2014 at the earliest.

Moreover, we cannot predict what healthcare reform initiatives may be adopted in the future. Further federal and state legislative and regulatory developments are likely, 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 product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop drug candidates.

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, testing, manufacturing and marketing of human therapeutic products. Product liability claims could delay or prevent completion of our clinical development programs. If we succeed in marketing products, such claims could result in an FDA investigation of the safety and effectiveness of our products, our manufacturing processes and facilities or our marketing programs, and potentially a recall of our products or more serious enforcement action, limitations on the approved indications for which they may be used, or suspension or withdrawal of approvals. Regardless of the merits or eventual outcome, liability claims may also result in injury to our reputation, costs to defend the related litigation, a diversion of management s time and our resources, and substantial monetary awards to trial participants or patients.

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 product 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.

Table of Contents

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

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

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

Risks Related to Patents, Licenses and Trade Secrets

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

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

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

Our pending patent applications may not result in issued patents. The patent position of pharmaceutical or biotechnology companies, including ours, is generally uncertain and involves complex legal and factual considerations. The standards that the USPTO and its foreign counterparts use to grant patents are not always applied predictably or uniformly and can change. Similarly, the ultimate degree of protection that will be afforded to biotechnology inventions, including ours, in the United States and foreign countries, remains uncertain and is dependent upon the scope of the protection decided upon by patent offices, courts and lawmakers.

Table of Contents

Moreover, there are periodic discussions in the Congress of the United States and in international jurisdictions about modifying various aspects of patent law. If any such changes are enacted and do not provide adequate protection for discoveries, including our ability to pursue infringers of our patents for substantial damages, our business could be adversely affected. There is also no uniform, worldwide policy regarding the subject matter and scope of claims granted or allowable in pharmaceutical or biotechnology patents. Accordingly, we do not know the degree of future protection for our proprietary rights or the breadth of claims that will be allowed in any patents issued to us or to others.

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

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

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

Our success will depend in part on the ability of our licensors to obtain, maintain and enforce patent protection for our licensed intellectual property, in particular, those patents to which we have secured exclusive rights. Our licensors may not successfully prosecute the patent applications to which we are licensed. Even if patents issue in respect of these patent applications, our licensors may fail to maintain these patents, may determine not to pursue litigation against other companies that are infringing these patents, or may pursue such litigation less aggressively than we would. Without protection for the intellectual property we license, other companies might be able to offer substantially identical products for sale, which could adversely affect our competitive business position and harm our business prospects. In addition, we sublicense our rights under various third-party licenses to our collaborators. Any impairment of these sublicensed rights could result in reduced revenues under our collaboration agreements or result in termination of an agreement by one or more of our collaborators.

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

RNAi is a relatively new scientific field, the commercial exploitation of which has resulted in many different patents and patent applications from organizations and individuals seeking to obtain patent protection in the field. We have obtained grants and issuances of RNAi patents and have licensed many of these patents from third parties on an exclusive basis. The issued patents and pending patent applications in the United States and in key markets around the world that we own or license claim many different methods, compositions and processes relating to the discovery, development, manufacture and commercialization of RNAi therapeutics.

Specifically, we have a portfolio of patents, patent applications and other intellectual property covering: fundamental aspects of the structure and uses of siRNAs, including their manufacture and use as therapeutics, and RNAi-related mechanisms; chemical modifications to siRNAs that improve their suitability for therapeutic uses; siRNAs directed to specific targets as treatments for particular diseases; and delivery technologies, such as in the field of cationic liposomes.

As the field of RNAi therapeutics is maturing, patent applications are being fully processed by national patent offices around the world. There is uncertainty about which patents will issue, and, if they do, as to when, to whom, and with what claims. It is likely that there will be significant litigation and other proceedings, such as interference, reexamination and opposition proceedings, in various patent offices relating to patent rights in the RNAi field. For example, various third parties have initiated oppositions to patents in our Kreutzer-Limmer and Tuschl II series in the EPO and in other jurisdictions. We expect that additional oppositions will be filed in the EPO and elsewhere, and other challenges will be raised relating to other patents and patent applications in our portfolio. In many cases, the possibility of appeal exists for either us or our opponents, and it may be years before final, unappealable rulings are made with respect to these patents in certain jurisdictions. The timing and outcome of these and other proceedings is

uncertain and may adversely affect our business if we are not successful in defending the patentability and scope of our pending and issued patent claims. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material adverse effect on our business and our ability to successfully compete in the field of RNAi.

Table of Contents

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

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

Third parties may sue us for infringing their patent rights. Likewise, we may need to resort to litigation to enforce a patent issued or licensed to us or to determine the scope and validity of proprietary rights of others. In addition, a third party may claim that we have improperly obtained or used its confidential or proprietary information. For example, in March 2011, Tekmira and Protiva filed a civil complaint in the Business Litigation Section of the Suffolk County Superior Court, in Boston, Massachusetts against us and on June 3, 2011, the plaintiffs filed an amended complaint adding AlCana, a research collaborator of ours, as a defendant. The amended complaint alleges misappropriation of the plaintiffs confidential and proprietary information and trade secrets, civil conspiracy, and tortious interference with contractual relationships by us and AlCana, and unjust enrichment, contractual breach, breach of the implied covenant of good faith and fair dealing, unfair competition, false advertising, unfair and deceptive trade practices by us, and seeks injunctive relief and unspecified damages and other relief. In April 2011, we served and filed an answer to the plaintiffs original complaint denying the plaintiffs claims in this action, together with counterclaims against the plaintiffs. In June 2011, we served and filed an answer to the plaintiffs amended complaint denying the plaintiffs claims and counterclaims against the plaintiffs asserting breach of contract, defamation, breach of covenant not to sue, breach of patent prosecution and non-use provisions, misappropriation of confidential and proprietary information and trade secrets, unjust enrichment, breach of the implied covenant of good faith and fair dealing, as well as violations of Massachusetts statutes. We are seeking the dismissal of the plaintiffs claims and judgment in our favor, as well as damages and equitable relief. Although we believe we have meritorious defenses to each of the claims in this lawsuit and intend to fully defend ourselves in this matter, litigation is subject to inherent uncertainty and a court could ultimately rule against us and award substantial damages. In addition, defense of litigation and related matters are costly and may divert the attention of our management and other resources that would otherwise be engaged in running our business.

Furthermore, third parties may challenge the inventorship of our patents or licensed patents. For example, in March 2011, the University of Utah filed a complaint in the United States District Court for the District of Massachusetts against us, Max Planck, Whitehead, MIT and UMass, claiming that a professor of the University is the sole inventor, or in the alternative, a joint inventor of certain of our in-licensed patents. The original complaint was not served on any of the parties and, in July 2011, the University filed an amended complaint containing substantially the same claims as the original complaint against us, Max Planck, Whitehead, MIT and UMass. The amended complaint alleges the defendants have incorrectly determined inventorship of some of our in-licensed patents and further claims unjust enrichment, unfair competition, false advertising and seeks correction of inventorship, injunctive relief and unspecified damages. We believe we have meritorious defenses against each of the claims in this lawsuit and intend to fully defend ourselves in this matter if the complaint is served. However, litigation is subject to inherent uncertainty and a court could ultimately rule against us.

In addition, in connection with a license agreement, we 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 delay our research and development efforts and 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.

Table of Contents

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

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

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

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

Risks Related to Competition

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

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

- much greater financial, technical and human resources than we have at every stage of the discovery, development, manufacture and commercialization of products;
- more extensive experience in pre-clinical testing, conducting clinical trials, obtaining regulatory approvals, and in manufacturing, marketing and selling pharmaceutical products;
- 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 ATTR, severe hypercholesterolemia, refractory anemia, RSV, liver cancers and HD, and have a number of additional discovery programs targeting other diseases. These drugs may be more effective, safer, less expensive, or marketed and sold more effectively, than any products we develop.

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

Table of Contents

the safety and effectiveness of our products;

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

the timing and scope of regulatory approvals for these products;

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

price;

reimbursement coverage; and

patent position.

Our competitors may develop or commercialize products with significant advantages over any products we develop based on any of the factors listed above or on other factors. Our competitors may therefore be more successful in commercializing their products than we are, which could adversely affect our competitive position and business. Competitive products may make any products we develop obsolete or noncompetitive before we can recover the expenses of developing and commercializing our product candidates. Such competitors could also recruit our employees, which could negatively impact our level of expertise and the ability to execute on our business plan. 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 product candidates noncompetitive, obsolete or uneconomical.

We face competition from other companies that are working to develop novel drugs and technology platforms using technology similar to ours. If these companies develop drugs more rapidly than we do or their technologies, including delivery technologies, are more effective, our ability to successfully commercialize drugs may 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 multiple companies that are working in the field of RNAi. In addition, we granted licenses or options for licenses to Isis, GeneCare Research Institute Co., Ltd., Benitec Ltd., Calando Pharmaceuticals, Inc., Tekmira, Quark Biotech, Inc. and others under which these companies may independently develop RNAi therapeutics against a limited number of targets. Any of these companies may develop its RNAi technology more rapidly and more effectively than us. Merck & Co., Inc., or Merck, was one of our collaborators and a licensee under our intellectual property for specified disease targets until September 2007, at which time we and Merck agreed to terminate our collaboration. As a result of its acquisition of Sirna Therapeutics, Inc. in December 2006, and in light of the mutual termination of our collaboration, Merck, which has substantially more resources and experience in developing drugs than we do, may become a direct competitor.

In addition, as a result of agreements that we have entered into, Roche and Takeda have obtained non-exclusive licenses, and Novartis has obtained specific exclusive licenses for 31 gene targets, to certain aspects of our technology that give them the right to compete with us in certain circumstances.

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

In addition to competition with respect to RNAi and with respect to specific products, we face substantial competition to discover and develop safe and effective means to deliver siRNAs to the relevant cell and tissue types.

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

Table of Contents

Our Alnylam Biotherapeutics efforts will also face competition from established companies developing and commercializing technology applications to improve the manufacturing processes for drugs. If these companies advance and market their technologies more rapidly than Alnylam Biotherapeutics, we may be unable to establish collaborations for Alnylam Biotherapeutics with established biologic manufacturers, selling licenses, products and services.

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

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

At June 30, 2011, Novartis held 13.1% of our outstanding common stock and has the right to maintain its ownership percentage until the earlier of any sale by Novartis of shares of our common stock and the expiration or termination of our collaboration and license agreement, subject to certain exceptions. 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.

Sales of additional shares of our common stock could result in dilution to existing stockholders and cause the price of our common stock to decline.

Sales of substantial amounts of our common stock in the public market, or the availability of such shares for sale, by us or others could adversely affect the price of our common stock. Novartis has rights, subject to certain conditions, to require us to file registration statements covering its shares or to include its shares in registration statements that we file, including the shelf registration statement we filed in July 2011. In addition, if Novartis decides to sell a portion of its shares in a rapid or disorderly manner, our stock price could be negatively impacted.

Table of Contents

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

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

a classified board of directors;

a prohibition on actions by our stockholders by written consent;

limitations on the removal of directors; and

advance notice requirements for election to our board of directors and for proposing matters that can be acted upon at stockholder meetings.

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

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

ITEM 5. OTHER INFORMATION.

As we previously reported, in a non-binding advisory vote at our 2011 Annual Meeting of Stockholders, a majority of the votes cast voted in favor of an annual advisory stockholder vote on the compensation of our named executive officers. After taking into consideration these voting results and our board of director s recommendation in favor of an annual advisory stockholder vote on the compensation of our named executive officers, we intend to hold future advisory votes on the compensation of our named executive officers every year.

Table of Contents

ITEM 6. EXHIBITS.

10.1	Sponsored Research Agreement dated as of July 27, 2009 by and among the Company, The University of British Columbia and AlCana Technologies, Inc. (filed as Exhibit 10.1 to the Registrant s Current Report on Form 8-K filed on June 29, 2011 (File No. 000-50743) and incorporated herein by reference).
10.2	Supplemental Agreement effective July 27, 2009 by and among the Company, Tekmira Pharmaceuticals Corporation, Protiva Biotherapeutics Inc., The University of British Columbia and AlCana Technologies, Inc. (filed as Exhibit 10.2 to the Registrant s Current Report on Form 8-K filed on June 29, 2011 (File No. 000-50743) and incorporated herein by reference).
12#	Computation of Consolidated Ratios of Earnings/Deficiencies to Fixed Charges.
31.1#	Certification of principal executive officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
31.2#	Certification of principal financial officer pursuant to Rule 13a-14(a) promulgated under the Securities Exchange Act of 1934, as amended.
32.1#	Certification of principal executive officer pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code.
32.2#	Certification of principal financial officer pursuant to Rule 13a-14(b) promulgated under the Securities Exchange Act of 1934, as amended, and Section 1350 of Chapter 63 of Title 18 of the United States Code.
101+	The following materials from Registrant s Quarterly Report on Form 10-Q for the quarter ended June 30, 2011, formatted in XBRL (Extensible Business Reporting Language): (i) the Condensed Consolidated Balance Sheets, (ii) the Condensed Consolidated Statements of Operations and Comprehensive Loss, (iii) the Condensed Consolidated Statements of Cash Flows, and (iv) Notes to Condensed Consolidated Financial Statements, tagged as blocks of text.

Indicates confidential treatment requested as to certain portions, which portions were omitted and filed separately with the Securities and Exchange Commission pursuant to a Confidential Treatment Request.

Filed herewith.

+ Furnished herewith.

Table of Contents

SIGNATURES

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

ALNYLAM PHARMACEUTICALS, INC.

Date: August 3, 2011 /s/ John M. Maraganore

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

Date: August 3, 2011 /s/ Michael P. Mason

Michael P. Mason
Vice President of Finance and Treasurer
(Principal Financial and Accounting Officer)