

ALNYLAM PHARMACEUTICALS, INC.

Form 10-Q

November 07, 2013

[Table of Contents](#)

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-Q

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

For the quarterly period ended September 30, 2013

OR

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

For the transition period from _____ to _____

Commission File Number 000-50743

ALNYLAM PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

77-0602661
(I.R.S. Employer
Identification No.)

300 Third Street, Cambridge, MA
(Address of Principal Executive Offices)
(617) 551-8200

02142
(Zip Code)

(Registrant's Telephone Number, Including Area Code)

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

Indicate by check mark whether the registrant 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 ☒ No ☐

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 ☐ Accelerated filer ☒

Non-accelerated filer ☐ (do not check if a smaller reporting company) 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 ☐ No ☒

At October 31, 2013, the registrant had 63,430,076 shares of Common Stock, \$0.01 par value per share, outstanding.

Table of Contents

INDEX

	PAGE NUMBER
PART I. FINANCIAL INFORMATION	
ITEM 1. FINANCIAL STATEMENTS (Unaudited)	
<u>CONDENSED CONSOLIDATED BALANCE SHEETS AS OF SEPTEMBER 30, 2013 AND DECEMBER 31, 2012</u>	2
<u>CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS FOR THE THREE AND NINE MONTHS ENDED SEPTEMBER 30, 2013 AND 2012</u>	3
<u>CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS FOR THE NINE MONTHS ENDED SEPTEMBER 30, 2013 AND 2012</u>	4
<u>NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS</u>	5
<u>ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS</u>	15
<u>ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK</u>	30
<u>ITEM 4. CONTROLS AND PROCEDURES</u>	30
PART II. OTHER INFORMATION	
<u>ITEM 1. LEGAL PROCEEDINGS</u>	31
<u>ITEM 1A. RISK FACTORS</u>	32
<u>ITEM 6. EXHIBITS</u>	52
<u>SIGNATURES</u>	53

Table of Contents

ALNYLAM PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS

(In thousands, except share and per share amounts)

(Unaudited)

	September 30, 2013	December 31, 2012
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 11,840	\$ 51,405
Marketable securities	181,939	71,407
Billed and unbilled collaboration receivables	609	104
Prepaid expenses and other current assets	4,776	2,641
Total current assets	199,164	125,557
Marketable securities	173,366	103,416
Investment in equity securities of Regulus Therapeutics Inc.	57,999	38,748
Property and equipment, net	16,974	19,799
Total assets	\$ 447,503	\$ 287,520

LIABILITIES AND STOCKHOLDERS EQUITY

Current liabilities:		
Accounts payable	\$ 2,728	\$ 4,420
Accrued expenses	15,386	11,558
Accrued intraperiod tax allocation	2,023	
Deferred rent	1,200	950
Deferred revenue	33,558	31,417
Total current liabilities	54,895	48,345
Deferred rent, net of current portion	3,247	4,248
Deferred revenue, net of current portion	91,779	100,874
Total liabilities	149,921	153,467
Commitments and contingencies (Note 3)		
Stockholders equity:		
Preferred stock, \$0.01 par value, 5,000,000 shares authorized and no shares issued and outstanding at September 30, 2013 and December 31, 2012		
Common stock, \$0.01 par value, 125,000,000 shares authorized; 63,236,216 shares issued and outstanding at September 30, 2013; 52,489,936 shares issued and outstanding at December 31, 2012	632	525

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

Additional paid-in capital	833,660	624,876
Accumulated other comprehensive income	27,168	15,662
Accumulated deficit	(563,878)	(507,010)
Total stockholders' equity	297,582	134,053
Total liabilities and stockholders' equity	\$ 447,503	\$ 287,520

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

[Table of Contents](#)**ALNYLAM PHARMACEUTICALS, INC.****CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS****(In thousands, except per share amounts)****(Unaudited)**

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2013	2012	2013	2012
Net revenues from research collaborators	\$ 8,991	\$ 16,759	\$ 36,320	\$ 58,230
Operating expenses:				
Research and development ⁽¹⁾	34,457	22,094	80,851	64,891
General and administrative ⁽¹⁾	6,768	12,812	18,819	34,446
Total operating expenses	41,225	34,906	99,670	99,337
Loss from operations	(32,234)	(18,147)	(63,350)	(41,107)
Other income (expense):				
Equity in loss of joint venture (Regulus Therapeutics Inc.)		(1,613)		(3,641)
Interest income	290	261	784	755
Other (expense) income	(12)	(3)	(18)	167
Total other income (expense)	278	(1,355)	766	(2,719)
Loss before income taxes	(31,956)	(19,502)	(62,584)	(43,826)
Benefit from income taxes	2,270		5,716	
Net loss	\$ (29,686)	\$ (19,502)	\$ (56,868)	\$ (43,826)
Net loss per common share - basic and diluted	\$ (0.48)	\$ (0.38)	\$ (0.93)	\$ (0.88)
Weighted average common shares used to compute basic and diluted net loss per common share	62,416	51,542	61,103	49,772
Comprehensive loss:				
Net loss	\$ (29,686)	\$ (19,502)	\$ (56,868)	\$ (43,826)
Unrealized (loss) gain on marketable securities, net of tax	(962)	170	11,506	273
Comprehensive loss	\$ (30,648)	\$ (19,332)	\$ (45,362)	\$ (43,553)

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

Research and development	\$ 6,805	\$ 2,271	\$ 11,092	\$ 6,357
General and administrative	2,040	1,115	4,205	3,281

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)**

	Nine Months Ended September 30,	
	2013	2012
Cash flows from operating activities:		
Net loss	\$ (56,868)	\$ (43,826)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	7,602	7,011
Non-cash stock-based compensation	15,297	9,638
Charge for 401(k) company stock match	351	310
Equity in loss of joint venture (Regulus Therapeutics Inc.)		3,641
Realized gain on sale of marketable securities		(179)
Benefit from intraperiod tax allocation on marketable securities	(5,716)	
Changes in operating assets and liabilities:		
Proceeds from landlord tenant improvements	192	1,214
Billed and unbilled collaboration receivables	(505)	(450)
Prepaid expenses and other assets	(2,222)	(1,359)
Accounts payable	(1,336)	(707)
Accrued expenses and other	3,871	2,678
Deferred revenue	(6,954)	(24,668)
Net cash used in operating activities	(46,288)	(46,697)
Cash flows from investing activities:		
Purchases of property and equipment	(3,128)	(7,662)
Increase in restricted cash		(162)
Purchases of marketable securities	(335,197)	(195,672)
Sales and maturities of marketable securities	151,772	163,357
Net cash used in investing activities	(186,553)	(40,139)
Cash flows from financing activities:		
Proceeds from exercise of stock options and other types of equity	19,819	5,974
Proceeds from issuance of common stock, net of offering costs	173,572	86,800
Payments for repurchase of common stock for employee tax withholding	(115)	(328)
Net cash provided by financing activities	193,276	92,446
Net (decrease) increase in cash and cash equivalents	(39,565)	5,610
Cash and cash equivalents, beginning of period	51,405	70,228

Cash and cash equivalents, end of period	\$	11,840	\$	75,838
--	----	--------	----	--------

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 state 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, 2012, 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 19, 2013. 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 Alnylam U.S., Inc., Alnylam Europe AG, Alnylam (Bermuda) Ltd. and Alnylam Securities Corporation, which are wholly-owned subsidiaries of the Company. All significant intercompany accounts and transactions have been eliminated.

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

The Company computes basic net loss per common share by dividing net loss by the weighted average number of common shares outstanding. The Company computes diluted net loss per common share by dividing net loss 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 Nine Months Ended September 30,	
	2013	2012
Options to purchase common stock	8,021	8,156
Unvested restricted common stock	593	638
	8,614	8,794

Restricted Stock Awards

In January 2012, as part of its post-restructuring retention program, the Company granted an aggregate of 508,928 shares of restricted stock to its retained employees, excluding the Company's chief executive officer and president and chief operating officer. These restricted stock awards were valued at \$5.3 million on the grant date and vest in full on the second anniversary of the grant date.

Table of Contents

The Company recognized an aggregate of \$1.3 million and \$0.7 million of stock-based compensation expense related to all outstanding restricted stock awards for the three months ended September 30, 2013 and 2012, respectively. The Company recognized an aggregate of \$2.6 million and \$1.9 million of stock-based compensation expense related to all outstanding restricted stock awards for the nine months ended September 30, 2013 and 2012, respectively.

Public Offering

In February 2012, the Company sold an aggregate of 8,625,000 shares of its common stock through an underwritten public offering at a price to the public of \$10.75 per share. As a result of the offering, the Company received aggregate net proceeds of approximately \$86.8 million, after deducting underwriting discounts and commissions and other estimated offering expenses of approximately \$5.9 million.

In January 2013, the Company sold an aggregate of 9,200,000 shares of its common stock through an underwritten public offering at a price to the public of \$20.13 per share. As a result of this offering, the Company received aggregate net proceeds of approximately \$173.6 million, after deducting underwriting discounts and commissions and other estimated offering expenses of approximately \$11.6 million.

Fair Value Measurements

The following tables present information about the Company's assets that are measured at fair value on a recurring basis at September 30, 2013 and December 31, 2012, 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. The fair value hierarchy level is determined by the lowest level of significant input. Financial assets measured at fair value on a recurring basis are summarized as follows, in thousands:

Description	At September 30, 2013	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	\$ 10,515	\$ 10,515	\$	\$
Marketable securities (fixed income)				
Corporate notes	266,418		266,418	
U.S. Government obligations	69,901		69,901	
Commercial paper	18,986		18,986	
Marketable securities (Regulus equity holdings)	57,999		57,999	
Total	\$ 423,819	\$ 10,515	\$ 413,304	\$

Description	At December 31,	Quoted Prices in Active	Significant Observable	Significant Unobservable
--------------------	----------------------------	------------------------------------	-----------------------------------	-------------------------------------

	2012	Markets (Level 1)	Inputs (Level 2)	Inputs (Level 3)
Cash equivalents	\$ 50,213	\$ 50,213	\$	\$
Marketable securities (fixed income)				
Corporate notes	91,523		91,523	
U.S. Government obligations	60,661		60,661	
Commercial paper	22,639		22,639	
Marketable securities (Regulus equity holdings)	38,748		38,748	
Total	\$ 263,784	\$ 50,213	\$ 213,571	\$

During the nine months ended September 30, 2013, there were no transfers between Level 1, Level 2 and Level 3 financial assets. 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.

Table of Contents***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 accumulated other comprehensive loss, a component of stockholders' equity. Realized gains and losses are determined using the specific identification method and are included in other income. The Company did not recognize any realized gains or losses from sales of its available-for-sale securities during the nine months ended September 30, 2013, and as a result, did not reclassify any amount out of accumulated other comprehensive income for the same period. 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 comprehensive loss. 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. At September 30, 2013, the Company's cash equivalents are composed of money market funds.

In the fourth quarter of 2012, the Company began accounting for its investment in Regulus Therapeutics Inc. (Regulus) as an available-for-sale marketable security. Intraperiod tax allocation rules require the Company to allocate its provision for income taxes between continuing operations and other categories of earnings, such as other comprehensive income. In periods in which the Company has a year-to-date pre-tax loss from continuing operations and pre-tax income in other categories of earnings, such as other comprehensive income, the Company must allocate the tax provision to the other categories of earnings. The Company then records a related tax benefit in continuing operations. The following tables summarize the fair value, accumulated other comprehensive income and intraperiod tax allocation regarding the Company's investment in Regulus available-for-sale marketable securities at September 30, 2013 and the activity for the three and nine months ended September 30, 2013, in thousands:

Description	At June 30, 2013	Three Months Ended September 30, 2013	Balance at September 30, 2013
Carrying value	\$ 12,449	\$	\$ 12,449
Accumulated other comprehensive income (loss), before tax	47,887	(2,337)	45,550
Investment in equity securities of Regulus Therapeutics Inc., as reported	\$ 60,336	\$ (2,337)	\$ 57,999
Accumulated other comprehensive income (loss), before tax	\$ 47,887	\$ (2,337)	\$ 45,550
	(14,018)	(2,270)	(16,288)

Intraperiod tax allocation recorded as a benefit from income taxes			
Intraperiod tax allocation recorded as an accrued liability	(5,232)	3,209	(2,023)
Accumulated other comprehensive income, net of tax	\$ 28,637	\$ (1,398)	\$ 27,239

Description	At December 31, 2012	Nine Months Ended September 30, 2013	Balance at September 30, 2013
Carrying value	\$ 12,449	\$	\$ 12,449
Accumulated other comprehensive income, before tax	26,299	19,251	45,550
Investment in equity securities of Regulus Therapeutics Inc., as reported	\$ 38,748	\$ 19,251	\$ 57,999
Accumulated other comprehensive income, before tax	\$ 26,299	\$ 19,251	\$ 45,550
Intraperiod tax allocation recorded as a benefit from income taxes	(10,572)	(5,716)	(16,288)
Intraperiod tax allocation recorded as an accrued liability		(2,023)	(2,023)
Accumulated other comprehensive income, net of tax	\$ 15,727	\$ 11,512	\$ 27,239

The Company obtains fair value measurement data for its fixed income marketable securities from independent pricing services. The Company performs validation procedures to ensure the reasonableness of this data. This includes meeting with the

Table of Contents

independent pricing services to understand the methods and data sources used. Additionally, the Company performs its own review of prices received from the independent pricing services by comparing these prices to other sources and confirming those securities are trading in active markets.

The following tables summarize the Company's fixed income marketable securities at September 30, 2013 and December 31, 2012, in thousands:

	September 30, 2013			
	Amortized	Gross	Gross	Fair
	Cost	Unrealized	Unrealized	Value
		Gains	Losses	
Commercial paper (Due within 1 year)	\$ 18,987	\$ 3	\$ (4)	\$ 18,986
Corporate notes (Due within 1 year)	148,864	46	(42)	148,868
Corporate notes (Due after 1 year through 2 years)	117,644	20	(114)	117,550
U.S. Government obligations (Due within 1 year)	14,079	7		14,086
U.S. Government obligations (Due after 1 year through 2 years)	55,802	17	(4)	55,815
Total	\$ 355,376	\$ 93	\$ (164)	\$ 355,305

	December 31, 2012			
	Amortized	Gross	Gross	Fair
	Cost	Unrealized	Unrealized	Value
		Gains	Losses	
Commercial paper (Due within 1 year)	\$ 22,650	\$ 1	\$ (12)	\$ 22,639
Corporate notes (Due within 1 year)	41,249	23	(4)	41,268
Corporate notes (Due after 1 year through 2 years)	50,322	5	(72)	50,255
U.S. Government obligations (Due within 1 year)	7,500			7,500
U.S. Government obligations (Due after 1 year through 2 years)	53,168	2	(9)	53,161
Total	\$ 174,889	\$ 31	\$ (97)	\$ 174,823

Subsequent Events

The Company evaluated all events or transactions that occurred after September 30, 2013 through the date these condensed consolidated financial statements were issued. During this period, the Company did not have any material recognized or nonrecognized subsequent events.

Recent Accounting Pronouncements

In February 2013, the Financial Accounting Standards Board (FASB) issued amendments to the accounting guidance for presentation of comprehensive income to improve the reporting of reclassifications out of accumulated other comprehensive income. The amendments did not change the current requirements for reporting net income or other

comprehensive income, but require an entity to provide information about the amounts reclassified out of accumulated other comprehensive income by component. In addition, an entity is now required to present, either on the face of the statement where the net income is presented or in the notes, significant amounts reclassified out of accumulated other comprehensive income by the respective line items of net income but only if the amount reclassified is required under GAAP to be reclassified to net income in its entirety in the same reporting period. For other amounts that are not required under GAAP to be reclassified in their entirety to net income, an entity is required to cross-reference to other disclosures required under GAAP that provide additional detail about these amounts. For public companies, these amendments were effective prospectively for reporting periods beginning after December 15, 2012. The Company adopted this guidance on January 1, 2013. Other than a change in presentation, the adoption of this guidance did not have a material impact on the Company's condensed consolidated financial statements.

In July 2013, the FASB issued new accounting guidance specific to income taxes. The new guidance requires an entity to present an unrecognized tax benefit and a net operating loss carryforward, a similar tax loss, or a tax credit carryforward on a net basis as part of a deferred tax asset, unless the unrecognized tax benefit is not available to reduce the deferred tax asset component or would not be utilized for that purpose, then a liability would be recognized. The updated accounting guidance is effective for fiscal years beginning after December 15, 2013. The Company does not expect the adoption of this guidance to have a material impact on 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 September 30,		Nine Months Ended September 30,	
	2013	2012	2013	2012
Takeda	\$ 5,494	\$ 5,494	\$ 16,481	\$ 16,481
Monsanto	1,410	519	4,230	519
The Medicines Company	1,253		3,343	
Cubist		694	9,721	2,084
Roche/Arrowhead		9,330		37,318
Other	834	722	2,545	1,828
Total net revenues from research collaborators	\$ 8,991	\$ 16,759	\$ 36,320	\$ 58,230

Platform Alliances***Takeda Alliance***

In May 2008, the Company entered into a license and collaboration agreement (the "Takeda Agreement") with Takeda to pursue the development and commercialization of RNAi therapeutics. Under the Takeda Agreement, the Company granted to 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.

In consideration for the rights granted to Takeda under the Takeda 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 Agreement. In June 2008, Takeda paid the Company an upfront payment of \$100.0 million and agreed to pay to the Company an additional \$50.0 million 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, the "Technology Transfer Milestones"). If Takeda elects to expand its license to additional therapeutic areas, Takeda will be required to pay the Company \$50.0 million for each additional field selected, if any. In addition, for each RNAi therapeutic product developed by Takeda, its affiliates and sublicensees, the Company is entitled to receive specified development, regulatory and commercialization milestone payments, totaling up to \$171.0 million per product, together with up to a double-digit percentage royalty payment based on worldwide annual net sales, if any. The potential future milestone payments per product include up to \$26.0 million for the achievement of specified development milestones, up to \$40.0 million for the achievement of specified regulatory milestones and up to \$105.0 million for the achievement of

specified commercialization milestones. The Company could potentially earn the next milestone payment of \$2.0 million under the Takeda Agreement based upon the achievement of a specified pre-clinical event by Takeda for an RNAi therapeutic product. For purposes of potential future revenue recognition, the Company does not believe this milestone or any future milestones are substantive. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any additional milestone payments or any royalty payments from Takeda.

Pursuant to the Takeda 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, the Company has a right of first negotiation to participate with Takeda in the development and commercialization of licensed products in the United States. 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 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 also 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 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 a proportional performance model. As future milestones are achieved, if any, 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. At September 30, 2013, deferred revenue under the Takeda Agreement was \$36.3 million.

Monsanto Alliance

In August 2012, the Company and Monsanto Company (Monsanto) entered into a license and collaboration agreement (the Monsanto Agreement), pursuant to which the Company granted to Monsanto a worldwide, exclusive, royalty bearing right and license, including the right to grant sublicenses, to the Company s RNAi platform technology and intellectual property controlled by the Company as of the date of the Monsanto Agreement or during the 30 months thereafter, in the field of agriculture. The Monsanto Agreement also includes the transfer of technology from the Company to Monsanto and a collaborative research project (the Monsanto Discovery Collaboration). Under the Monsanto Agreement, Monsanto will be the Company s exclusive collaborator in the agriculture field for a ten-year period (the Exclusivity Period).

In consideration for the rights granted to Monsanto under the Monsanto Agreement, Monsanto paid the Company \$29.2 million in upfront cash payments. Monsanto is also required to make near-term milestone payments to the Company upon the achievement of specified technology transfer and patent-related milestones. The Company is also entitled to receive additional funding for collaborative research efforts. In the aggregate, the Company can earn up to \$5.0 million in potential future milestone payments and research funding under the Monsanto Agreement. In addition, Monsanto is required to pay to the Company a percentage of specified fees from certain sublicense agreements Monsanto may enter into that include access to the Company s intellectual property, as well as low single-digit royalty payments on worldwide, net sales by Monsanto, its affiliates and sublicensees of certain Licensed Products (as defined in the Monsanto Agreement), if any. In December 2012, the Company received a milestone payment of \$1.5 million of the \$5.0 million in potential milestone payments under the Monsanto Agreement based upon the achievement of a specified patent-related event. In August 2013, the Company received an additional milestone payment of \$2.5 million based upon the completion of technology transfer activities. The Company could potentially earn the next and final milestone payment of \$1.0 million under the Monsanto Agreement in connection with the Monsanto Discovery Collaboration. For purposes of potential future revenue recognition, the Company does not believe this final milestone is substantive. Due to the uncertainty of the application of RNAi technology in the field of agriculture, the Company may not receive the final milestone payment or any royalty payments from Monsanto.

The Company determined that the significant deliverables under the Monsanto Agreement include the license, the technology transfer activities and the services that the Company will be obligated to perform under the Monsanto Discovery Collaboration. The Company also determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the license and undelivered technical transfer activities and Monsanto Discovery Collaboration services do not have standalone value due to the specialized nature of the services to be provided by the Company. In addition, while Monsanto has the ability to grant sublicenses, it cannot grant access to certain of the Company's proprietary technology. The uniqueness of the Company's services and the limited sublicense right are indicators that standalone value is not present in the arrangement. Therefore the deliverables are not separable and, accordingly, the license and undelivered technical transfer activities and Monsanto Discovery Collaboration 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 model on the final deliverable. Under the Monsanto Agreement, the last deliverable to be completed is the Monsanto Discovery Collaboration, which must be completed within five years. The Company is recognizing revenue under the Monsanto Agreement on a straight-line basis over five years. The Company is not utilizing a proportional performance model since it is unable to reasonably estimate the level of effort to fulfill these obligations, primarily because the effort required under the Monsanto Discovery Collaboration is largely unknown.

Table of Contents

The Company received a payment of \$29.2 million from Monsanto in August 2012, which was initially recorded as deferred revenue. Under the terms of the Monsanto Agreement, in the event that during the Exclusivity Period the Company ceases to own or otherwise exclusively control certain licensed patent rights in the agriculture field, for any reason other than Monsanto's breach of the Monsanto Agreement or its negligence or willful misconduct, resulting in the loss of exclusivity with respect to Monsanto's rights to such patent rights, and such loss of exclusivity has a material adverse effect on the Licensed Products, then the Company would be required to pay Monsanto up to \$5.0 million as liquidated damages, and Monsanto's royalty obligations to the Company under the Monsanto Agreement would be reduced or, under certain circumstances, terminated. The Company has the right to cure any such loss of patent rights under the Monsanto Agreement. The Company has determined that this amount is not fixed and determinable and therefore, the Company has excluded this amount from its revenue model and is deferring the recognition of \$5.0 million of revenue. The Company will continue to reassess when this amount can be considered fixed and determinable. If the achievement of a milestone is considered probable at the inception of the collaboration, the Company's policy is to include the related payment in its revenue model. The Company concluded that the receipt of the technology transfer payment of \$2.5 million was probable, and has therefore included this amount in the Company's revenue model. As future milestones are achieved, if any, 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. At September 30, 2013, deferred revenue under the Monsanto Agreement was \$27.0 million.

Product Alliances

Cubist Alliance

In January 2009, the Company entered into a license and collaboration agreement with Cubist Pharmaceuticals, Inc. (the "Cubist Agreement") to develop and commercialize therapeutic 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 provided 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. In December 2010, the Company and Cubist jointly made a portfolio decision to put the development of ALN-RSV02 on hold. Pursuant to the terms of the Amendment, the Company continued to develop ALN-RSV01 for adult transplant patients at its sole discretion and expense and Cubist had the right to opt into collaborating with the Company on ALN-RSV01, subject to specified conditions.

In consideration for the rights granted to Cubist under the Cubist Agreement, in January 2009, Cubist paid the Company an upfront cash payment of \$20.0 million. Under the terms of the Cubist Agreement, the Company and Cubist shared responsibility for developing licensed products in North America and each was responsible for one-half of the related development costs, subject to the terms of the Amendment. The Company's collaboration with Cubist for the development of licensed products in North America was governed by a joint steering committee comprised of an equal number of representatives from each party.

The Company determined that the deliverables under the Cubist Agreement included the licenses, technology transfer related to the ALN-RSV program, the joint steering committee and the development and manufacturing services that the Company was obligated to perform during the development period. The Company also determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the licenses and undelivered services were not separable and, accordingly, the licenses and services were 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 was

the development and manufacturing services, which had an expected life of approximately eight years.

In February 2013, Cubist notified the Company that it would not exercise its opt-in right for ALN-RSV01. In light of this determination, the Company and Cubist mutually agreed to terminate the license and collaboration agreement effective as of February 6, 2013 (the "Cubist Effective Date"). As of the Cubist Effective Date, the parties have no further rights and obligations under the Cubist Agreement, as amended, notwithstanding anything to the contrary in the Cubist Agreement, as amended.

The Company was recognizing the upfront payment of \$20.0 million on a straight-line basis over approximately eight years because the Company was unable to reasonably estimate the level of effort to fulfill its performance obligations, and therefore, could

Table of Contents

not utilize a proportional performance model. As a result of the termination of the Cubist Agreement in February 2013 and the end of the Company's performance obligations thereunder, the Company recognized the remaining deferred revenue of \$9.7 million during the three months ended March 31, 2013.

Genzyme Alliance

In October 2012, the Company and Genzyme entered into a license and collaboration agreement (the "Genzyme Agreement") pursuant to which the Company granted to Genzyme an exclusive license in Japan and the Asia-Pacific region (the "Genzyme Territory") to develop and commercialize RNAi therapeutics targeting transthyretin ("TTR") for the treatment of transthyretin-mediated amyloidosis ("ATTR") and other human diseases. The Genzyme Agreement covers patisiran (the recommended International Nonproprietary Name ("INN") for ALN-TTR02) and ALN-TTRsc, and may in the future cover additional TTR-specific RNAi therapeutic compounds that comprise the Company's TTR program (together, "ALN-TTR Licensed Products"), subject, in the case of Improvement Products (as defined in the Genzyme Agreement), to specified additional terms and conditions. Under the Genzyme Agreement, the Company retains all development and commercialization rights worldwide outside of the Genzyme Territory.

In consideration for the rights granted to Genzyme under the Genzyme Agreement, Genzyme paid the Company an upfront cash payment of \$22.5 million. Upon achievement of certain milestones, the Company will be entitled to receive milestone payments, up to an aggregate of \$50.0 million, including up to \$25.0 million in specified development milestones and \$25.0 million in specified regulatory milestones. In addition, the Company will be entitled to tiered royalties expected to yield an effective royalty rate percentage ranging from the mid-teens to mid-twenties based on annual net sales, if any, of ALN-TTR Licensed Products in the Genzyme Territory by Genzyme, its affiliates and sublicensees. The Company could potentially earn the next development milestone payment of \$7.0 million under the Genzyme Agreement based upon the completion of a successful Phase II ALN-TTR clinical trial, as defined in the Genzyme Agreement. For purposes of potential future revenue recognition, the Company does not believe this milestone or any future milestones are substantive. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any milestone or royalty payments from Genzyme.

Under the Genzyme Agreement, the parties will collaborate in the development of ALN-TTR Licensed Products, with Genzyme assuming primary responsibility for the development and commercialization of ALN-TTR Licensed Products in the Genzyme Territory and the Company retaining primary responsibility for the development and commercialization of ALN-TTR Licensed Products in the rest of the world. The collaboration between Genzyme and the Company is governed by a joint steering committee that will be comprised of an equal number of representatives from each party. Under the agreement, Genzyme is establishing a development plan for the ALN-TTR program relating to the development activities to be undertaken in the Genzyme Territory. Genzyme 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 ATTR in the Genzyme Territory. The Company and Genzyme intend to enter into a supply agreement to provide for supply of ALN-TTR Licensed Products to Genzyme for clinical trials, and, at Genzyme's request, commercial sales. Genzyme may elect, at any time during the term of the Genzyme Agreement, to manufacture ALN-TTR Licensed Products itself or arrange for a third party to manufacture ALN-TTR Licensed Products.

Genzyme also has a right of first negotiation in the event that the Company desires to grant any third party rights to develop and/or commercialize an ALN-TTR Licensed Product for the treatment of ATTR or other human diseases outside of the Genzyme Territory.

The Genzyme Agreement originally provided that if development of an ALN-TTR Licensed Product was terminated by the Company or Genzyme under certain limited circumstances, Genzyme would have the right to terminate the Genzyme Agreement and the Company would be required to refund certain amounts paid by Genzyme to the Company under the Genzyme Agreement prior to such termination. In February 2013, the Company and Genzyme amended the Genzyme Agreement to remove this provision.

The Company has determined that the significant deliverables under the Genzyme Agreement include the license, the joint steering committee and any additional TTR-specific RNAi therapeutic compounds that comprise the ALN-TTR program. The Company also determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the license and undelivered joint steering committee and any additional TTR-specific RNAi therapeutic compounds do not have standalone value due to the specialized nature of the services to be provided by the Company. In addition, while Genzyme has the ability to grant sublicenses, it cannot sublicense all or substantially all of its rights under the Genzyme Agreement. The uniqueness of the Company's services and the limited sublicense right are indicators that standalone value is not present in the arrangement. Therefore the deliverables are not separable and, accordingly, the license and undelivered 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.

Table of Contents

The Company is currently unable to reasonably estimate its period of performance under the Genzyme Agreement, as it is unable to estimate the timeline of its deliverables related to the deliverable for any additional TTR-specific RNAi therapeutic compounds. The Company is deferring all revenue under the Genzyme 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 Genzyme Agreement. At September 30, 2013, deferred revenue under the Genzyme Agreement was \$22.5 million.

The Medicines Company Agreement

In February 2013, the Company and The Medicines Company (MDCO) entered into a license and collaboration agreement (the MDCO Agreement) pursuant to which the Company granted to MDCO an exclusive, worldwide license to develop, manufacture and commercialize RNAi therapeutics targeting proprotein convertase subtilisin/kexin type 9 (PCSK9), including ALN-PCS02 and ALN-PCSsc, for the treatment of hypercholesterolemia and other human diseases (collectively, ALN-PCS Licensed Products). ALN-PCS02 is an intravenously administered RNAi therapeutic for which the Company completed a Phase I clinical trial, and ALN-PCSsc is a subcutaneously administered RNAi therapeutic currently in pre-clinical development.

In consideration for the rights granted to MDCO under the MDCO Agreement, MDCO paid the Company an upfront cash payment of \$25.0 million. Upon achievement of certain milestones, the Company will be entitled to receive milestone payments, up to an aggregate of \$180.0 million, including up to \$30.0 million in specified development milestones, \$50.0 million in specified regulatory milestones and \$100.0 million in specified commercialization milestones. In addition, the Company will be entitled to scaled double-digit royalties based on annual worldwide net sales, if any, of ALN-PCS Licensed Products by MDCO, its affiliates and sublicensees, subject to reduction under specified circumstances. The Company could potentially earn the next development milestone payment of \$10.0 million under the MDCO Agreement based upon the initiation of the next clinical trial. For purposes of potential future revenue recognition, the Company does not believe this milestone or any future milestones are substantive. Due to the uncertainty of pharmaceutical development and the high historical failure rates generally associated with drug development, the Company may not receive any milestone or royalty payments from MDCO.

Under the MDCO Agreement, the parties will collaborate in the further development of ALN-PCS Licensed Products. The Company will retain responsibility for the development of ALN-PCS Licensed Products until Phase I Completion (as defined in the MDCO Agreement) at its cost, up to an agreed upon initial development cost cap. MDCO will assume all other responsibility for the development and commercialization of ALN-PCS Licensed Products, at its sole cost. Initially the collaboration included the development of both ALN-PCS02 and ALN-PCSsc in parallel. In October 2013, the parties announced the selection of ALN-PCSsc for ongoing development, in accordance with the terms of the MDCO Agreement. The collaboration between MDCO and the Company will be governed by a joint steering committee that will be comprised of an equal number of representatives from each party. The Company will be solely responsible for obtaining supply of finished product reasonably required for the conduct of its obligations through Phase I Completion, and supplying MDCO with finished product reasonably required for the first Phase II clinical trial of an ALN-PCS Licensed Product conducted by MDCO, at the Company's expense, provided such costs do not exceed the development costs cap, subject to certain exceptions. After such time, MDCO will have the sole right and responsibility to manufacture and supply ALN-PCS Licensed Product for development and commercialization under the MDCO development plan, subject to the terms of the MDCO Agreement. The Company also has obligations under the MDCO Agreement to transfer certain technology to MDCO.

The Company has determined that the significant deliverables under the MDCO Agreement include the license, the joint steering committee, technology transfer obligations, development activities through Phase I Completion and supply of product for a Phase II clinical trial. The Company also determined that, pursuant to the accounting guidance

governing revenue recognition on multiple element arrangements, the license and collective undelivered activities and services do not have standalone value due to the specialized nature of the activities and services to be provided by the Company. In addition, while MDCO has the ability to grant sublicenses, it must receive the Company's prior written consent to sublicense all or substantially all of its rights. The uniqueness of the Company's services and the limited sublicense right are indicators that standalone value is not present in the arrangement. Therefore the deliverables are not separable and, accordingly, the license and undelivered 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 MDCO Agreement, all deliverables are expected to be completed within five years. The Company is recognizing revenue under the MDCO Agreement on a straight-line basis over five years. The Company is not utilizing a proportional performance model since it is unable to reasonably estimate the level of effort to fulfill these obligations, primarily because the effort required under the development activities is largely unknown.

The Company received the upfront payment of \$25.0 million from MDCO in February 2013, which was initially recorded as deferred revenue. As future milestones are achieved, if any, 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. At September 30, 2013, deferred revenue under the MDCO Agreement was \$21.8 million.

Table of Contents

3. COMMITMENTS AND CONTINGENCIES

Litigation

University of Utah Litigation

On March 22, 2011, The University of Utah (*Utah*) filed a civil complaint in the United States District Court for the District of Massachusetts against the Company, Max Planck Gesellschaft Zur Foerderung 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 Utah is the sole inventor or, in the alternative, a joint inventor, of the Tuschl patents. Utah did not serve the original complaint on the Company or the other defendants. On July 6, 2011, Utah 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. Utah is seeking changes to the inventorship of the Tuschl patents, unspecified damages and other relief. On October 31, 2011, the Company, Max Planck, Whitehead, MIT and UMass filed a motion to dismiss. Also on October 31, 2011, UMass filed a motion to dismiss on separate grounds, which the Company, Max Planck, Whitehead and MIT have joined. On December 31, 2011, Utah filed a second amended complaint dropping UMass as a defendant and adding as defendants several UMass officials. In June 2012, the Court denied both motions to dismiss. The Company, Max Planck, Whitehead, MIT and UMass filed an appeal of the Court's ruling on the motion to dismiss for lack of jurisdiction and a motion requesting that the Court stay the case pending the outcome of the appeal. In July 2012, the Court stayed discovery in the case pending the outcome of the defendants' appeal. Oral arguments in the appeal were heard in early March 2013 in the United States Court of Appeals for the Federal Circuit (the *CAFC*). In August 2013, the CAFC affirmed the lower Court's ruling, in a split decision. The Company believes the majority made an error in law when affirming the lower Court's decision, and in September 2013, the Company filed a petition with the CAFC for rehearing or rehearing *en banc*. In October 2013, the CAFC invited Utah to file an answer to the petition. The Company is awaiting a decision on the petition.

Although the Company believes it has meritorious defenses and intends to vigorously defend itself in this matter, litigation is subject to inherent uncertainty and a court could ultimately rule against the Company. 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 other activities. The Company has not recorded an estimate of the possible loss associated with this legal proceeding due to the uncertainties related to both the likelihood and the amount of any possible loss or range of loss.

The Company's accounting policy for accrual of legal costs is to recognize such expenses as incurred.

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, as amended and Section 21E of the Securities Exchange Act of 1934, as amended. 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 expressly disclaim any 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 in this Item 2

Management's Discussion and Analysis of Financial Condition and Results of Operations, as well as under 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 a variety of diseases.

Our core product strategy, which we refer to as Alnylam 5x15, is focused on the development and commercialization of novel RNAi therapeutics for the treatment of genetically defined targets for diseases with high unmet medical need. Under our core product strategy, we expect to have five RNAi therapeutic programs in clinical development, including programs in advanced stages, on our own or with one or more collaborators, 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 are currently advancing multiple core programs in clinical or pre-clinical development: ALN-TTR, comprised of patisiran (the recommended International Nonproprietary Name, or INN, for ALN-TTR02) and ALN-TTRsc, for the treatment of transthyretin-mediated amyloidosis, or ATTR; ALN-AT3 for the treatment of hemophilia and rare bleeding disorders, or RBD; ALN-AS1 for the treatment of porphyria, including acute intermittent porphyria, or AIP; ALN-CC5 for the treatment of complement-mediated diseases; ALN-TMP for the treatment of beta-thalassemia and iron-overload disorders; and ALN-AAT for the treatment of alpha-1-antitrypsin, or AAT, deficiency-associated liver disease. We intend to focus on developing and commercializing certain programs on our own in North and South America, Europe and other parts of the world. In February 2013, we entered into a global alliance with The Medicines Company, or MDCO, to advance our ALN-PCS program for the treatment of hypercholesterolemia. We may enter into alliances to

advance certain other programs in the future.

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 two partner-based clinical-stage programs, ALN-RSV01 for the treatment of respiratory syncytial virus, or RSV, infection, and ALN-VSP for the treatment of liver cancers, as well as one candidate in pre-clinical development, ALN-HTT, for the treatment of Huntington's disease, or HD.

We also continue to work internally and with third-party collaborators with the goal of developing new, or optimizing existing, 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 academic and corporate third parties, as well as government entities, to evaluate and optimize different delivery options.

We believe that the strength of our intellectual property portfolio relating to the development and commercialization of small interfering RNAs, or siRNAs, as therapeutics provides us a leading position with respect to this therapeutic modality. Our intellectual

Table of Contents

property portfolio 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 pharmaceutical and life sciences companies, including Isis Pharmaceuticals, Inc., or Isis, Medtronic, Inc., or Medtronic, Novartis Pharma AG, or Novartis, Biogen Idec Inc., or Biogen Idec, F. Hoffmann-La Roche Ltd, or Roche (which assigned its rights and obligations to Arrowhead Research Corporation, or Arrowhead, during 2011), Takeda Pharmaceutical Company Limited, or Takeda, Kyowa Hakko Kirin Co., Ltd., or Kyowa Hakko Kirin, Cubist Pharmaceuticals, Inc., or Cubist, Ascleptis Pharmaceuticals (Hangzhou) Co., Ltd., or Ascleptis, Monsanto Company, or Monsanto, Genzyme Corporation, or Genzyme, and MDCO. We have previously entered, and in the future, we may enter, into contracts with government agencies. We also have established collaborations with and, in some instances, received funding from major medical and disease associations, including CHDI Foundation, Inc. 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 InterferRx 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. In 2007, we and Isis established Regulus Therapeutics Inc., or Regulus, a company focused on the discovery, development and commercialization of microRNA therapeutics. In October 2012, Regulus completed its initial public offering, and in July 2013, Regulus completed an additional underwritten public offering. Currently, we own approximately 15% of Regulus outstanding common stock. Through an internal effort we refer to as Alnylam Biotherapeutics, we are advancing the application of RNAi technology to improve the manufacturing processes for biologics, including recombinant proteins and monoclonal antibodies. We have formed, and may form additional, collaborations through this effort with third-party biopharmaceutical companies. In October 2011, we entered into a collaboration with GlaxoSmithKline, or GSK, for influenza vaccine production, with our VaxiRNA platform, an RNAi technology developed under our Alnylam Biotherapeutics initiative, for the enhanced production of viruses used in the manufacture of vaccine products.

In January 2012, we implemented a strategic corporate restructuring pursuant to which we reduced our overall workforce by approximately 33%, to approximately 115 employees. The reduction in personnel costs, along with other external costs, resulted in significant savings in our 2012 operating expenses. The workforce reduction was substantially completed at the end of the first quarter of 2012. During the three months ended March 31, 2012, we substantially completed the implementation of the strategic corporate restructuring and recorded \$3.9 million of restructuring-related costs in operating expenses, including employee severance, benefits and related costs. We paid substantially all of these restructuring costs during 2012. We do not expect to incur any additional significant costs associated with this restructuring.

In November 2012, we, Tekmira Pharmaceuticals Corporation, or TPC, Protiva Biotherapeutics, Inc., or Protiva, a wholly-owned subsidiary of TPC, and together with TPC, referred to as Tekmira, and Acuitas Therapeutics Inc. (formerly AlCana Technologies, Inc.), or Acuitas, entered into a settlement agreement and general release resolving all ongoing litigation between the parties, as well as a patent interference proceeding between us and Protiva. The terms of the settlement agreement include mutual releases and dismissal with prejudice of all claims and counterclaims in connection with all of the litigation pending between the parties. Contemporaneously with the

execution of the settlement agreement, we and Tekmira restructured our contractual relationship and entered into a cross-license agreement that supersedes the prior license and manufacturing agreements among us, TPC and Protiva. In connection with this restructuring, we incurred a \$65.0 million charge to operating expenses for the year ended December 31, 2012.

We have incurred significant losses since we commenced operations in 2002 and expect such losses to continue for the foreseeable future. At September 30, 2013, we had an accumulated deficit of \$563.9 million. 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 and optimization 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. We anticipate that our operating results will fluctuate for the foreseeable future. Therefore, period-to-period comparisons should not be relied upon as predictive of the results in future periods.

Table of Contents

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. 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 sources of potential funding for the next several years to be derived primarily from new and existing strategic alliances, which may include license and other fees, funded research and development and milestone payments, and proceeds from the sale of equity or debt.

In December 2012, we filed an automatically effective shelf registration statement with the SEC for an indeterminate number of shares. In January 2013, we sold an aggregate of 9,200,000 shares of our common stock through an underwritten public offering at a price to the public of \$20.13 per share. As a result of the offering, we received aggregate net proceeds of approximately \$173.6 million, after deducting underwriting discounts and commissions and other estimated offering expenses of approximately \$11.6 million. We intend to use these proceeds for general corporate purposes, ultimately focused on advancing our clinical pipeline, and in particular our patisiran, ALN-TTRsc, ALN-AT3 and ALN-AS1 programs, as well as for potential acquisitions of new businesses, technologies or products, working capital, capital expenditures and general and administrative expenses.

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 have five RNAi therapeutic programs in clinical development by the end of 2015, including programs in advanced stages, on our own or with one or more collaborators. 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 and optimize technologies to deliver our RNAi therapeutics both directly to specific sites of disease, and systemically by intravenous or subcutaneous administration.

Our most advanced core product development program, ALN-TTR, targets the transthyretin, or TTR, gene, for the treatment of ATTR. ATTR is an inherited, progressively debilitating and fatal disease caused by a mutation in the TTR gene. In May 2012, we reported final clinical results from our ALN-TTR01 Phase I, multinational clinical trial showing that ALN-TTR01 was generally safe and well tolerated and resulted in statistically significant lowering of both wild-type and mutant TTR serum levels in ATTR patients. ALN-TTR01 employs a first-generation lipid nanoparticle, or LNP, formulation and the ALN-TTR01 Phase I clinical trial has provided proof-of-concept data for our ALN-TTR program.

We are advancing patisiran (the recommended INN for ALN-TTR02) as our lead product candidate in our ALN-TTR program. Patisiran uses the same siRNA as ALN-TTR01, and a second-generation LNP delivery technology. In July 2012, we reported positive clinical results from our patisiran Phase I clinical trial, which was conducted in the United Kingdom as a randomized, single-blind, placebo-controlled, single-ascending dose study, which enrolled 17 healthy volunteer subjects. The primary objective of the study was to evaluate the safety and tolerability of a single dose of patisiran. Secondary objectives of this study included the characterization of pharmacokinetics of patisiran and the assessment of clinical activity as measured by effects on serum TTR levels through at least day 56 following a single dose. Patisiran was found to be generally safe and well tolerated in this Phase I clinical trial, consistent with our broader clinical experience with LNP-formulated siRNAs.

In June 2013, we reported interim clinical results from our Phase II clinical trial of patisiran performed in ATTR patients with familial amyloidotic polyneuropathy, or FAP. The data were presented at the 2013 Biennial Meeting of

the Peripheral Nerve Society, or PNS. In September 2013, we reported that we have completed enrollment in this study. The Phase II clinical trial is an open-label, multi-center, multi-dose, dose-escalation trial to evaluate the safety and tolerability of two doses of patisiran and to demonstrate clinical activity based on serial measurement of circulating serum levels of wild-type and mutant TTR. This clinical trial enrolled 29 ATTR FAP patients with patisiran administered at doses of 0.01 to 0.30 mg/kg, using either a once-every-four-week or once-every-three-week dosing regimen.

As reported at the PNS meeting, interim data from the first 19 patients enrolled and analyzed in this study showed that multiple doses of patisiran resulted in rapid, dose-dependent and durable knockdown of serum TTR levels. As compared with the lowest dose group of 0.01 mg/kg, there was a statistically significant knockdown of serum TTR at doses of 0.15 mg/kg ($p < 0.01$) and 0.30 mg/kg ($p < 0.001$). At 0.30 mg/kg administered once every four weeks, mean TTR knockdown at nadir of 82.6% and 84.8% was observed following the first and second doses, respectively, and maximum TTR knockdown was up to 90.8%. At 0.30 mg/kg administered once every three weeks, mean TTR knockdown at nadir of 83.1% and 87.4% was observed following the first and second doses, respectively, and maximum TTR knockdown was up to 92.8%.

Table of Contents

As reported at the PNS meeting, multiple doses of patisiran were found to be generally safe and well tolerated. There were no significant adverse events or discontinuations associated with drug up through 0.30 mg/kg. There were no abnormalities in liver function tests, renal function or hematologic parameters. Adverse events included a mild infusion-related reaction that occurred in one patient who was able to complete dosing with slowing of the infusion rate. An episode of self-limiting cellulitis of the arm, a serious adverse event, occurred as a result of drug leakage at the infusion site in a patient with poor intravenous access.

In September 2013, we also announced that we have opened enrollment in an open-label extension, or OLE, study of patisiran for patients treated in the Phase II clinical trial. Patients will receive patisiran at a dose of 0.3 mg/kg every three weeks for up to two years. The primary objective of this clinical trial is to evaluate the long-term safety and tolerability of patisiran administration. In addition, the study will measure a number of clinical endpoints at baseline and every six months thereafter. This includes measurement of a modified composite neuropathy impairment score, or NIS, termed mNIS+7, which is an evaluation of muscle weakness, sensory and autonomic function and nerve conductance across a 304-point scale, where neuropathy progression leads to an increased score over time. A number of additional clinical endpoints will also be assessed. We expect to report initial data from the OLE study in 2014, with periodic updates thereafter approximately once a year. We expect to initiate a Phase III pivotal trial of patisiran in ATTR patients with FAP by the end of 2013.

The Committee for Orphan Medicinal Products of the European Medicines Agency has designated patisiran as an orphan medicinal product for the treatment of FAP. In addition, the United States Food and Drug Administration, or FDA, has also provided Orphan Drug Designation to patisiran as a therapeutic for the treatment of FAP.

In addition to patisiran (ALN-TTR02), we are advancing ALN-TTRsc, which utilizes our GalNAc-siRNA conjugate delivery platform enabling subcutaneous dose administration. In September 2013, we reported interim results from our ongoing Phase I clinical trial of ALN-TTRsc being conducted in the United Kingdom. The Phase I clinical trial is a randomized, double-blind, placebo-controlled, single- and multi-dose, dose-escalation trial, enrolling up to 40 healthy volunteer subjects. The primary objective of this study is to evaluate the safety and tolerability of single and multiple doses of subcutaneously administered ALN-TTRsc. Secondary objectives include assessment of clinical activity of the ALN-TTRsc as measured by serum TTR levels. In an initial single-ascending dose phase of the study, subjects (n=16) received subcutaneous doses of placebo or ALN-TTRsc from 1.25 to 10 mg/kg. In the multiple-ascending dose phase of the study, subjects (n=12) received 10 subcutaneous doses of placebo or ALN-TTRsc from 2.5 to 10 mg/kg. As reported in September 2013, interim data from the 28 subjects enrolled and analyzed in this study as of that date showed that single- and multi-dose administration of ALN-TTRsc resulted in rapid, dose-dependent, consistent, and durable knockdown of serum TTR levels. In the multi-dose cohorts (n=12), there was a statistically significant knockdown of serum TTR at doses of 2.5 mg/kg ($p<0.01$), 5.0 mg/kg ($p<0.001$) and 10.0 mg/kg ($p<0.001$) as compared to placebo. At a dose of 5.0 mg/kg, ALN-TTRsc administration resulted in an up to 93.3% knockdown of serum TTR and a mean TTR knockdown of 87.5% at nadir. At a dose of 10.0 mg/kg, ALN-TTRsc administration led to an up to 94.0% knockdown of serum TTR and a mean TTR knockdown of 92.4% at nadir. Analysis of the TTR knockdown in humans as compared to results obtained in non-human primates showed a closely correlated, essentially one-to-one relationship on a mg/kg basis ($r^2=0.83$, $p<0.001$). We believe these results confirm human translation for our GalNAc-siRNA conjugate platform, which is also being employed in the majority of our other programs.

In this study as reported in September 2013, single and multiple doses of ALN-TTRsc were found to be generally safe and well tolerated. There were no significant adverse events associated with drug at doses through 10.0 mg/kg. All adverse events were deemed mild or moderate in severity. Injection site reactions were observed in a minority of subjects receiving ALN-TTRsc (24%) or placebo (14%). These were reported as being clinically mild and consisted of transient erythema associated in a minority of cases with edema and/or pain. In all cases, these reactions were

self-limiting and resolved within approximately two hours of onset. There were no study discontinuations, flu-like symptoms, or changes in cytokines, C-reactive protein (CRP), liver function tests, renal function or hematologic parameters.

Upon completion of this Phase I trial, we expect to start a pilot Phase II clinical study of ALN-TTRsc in patients with familial amyloidotic cardiomyopathy, or FAC, and, if results are positive, plan to start a pivotal Phase III trial with ALN-TTRsc in FAC patients.

We intend to directly commercialize patisiran and ALN-TTRsc in North and South America, Europe and other parts of the world. In October 2012, we and Genzyme entered into a license and collaboration agreement pursuant to which we granted to Genzyme an exclusive license in Japan and the Asia-Pacific region, known as the Genzyme territory, to develop and commercialize specified RNAi therapeutics targeting TTR for the treatment of ATTR and other human diseases. We retain all development and commercialization rights worldwide outside of the Genzyme territory.

Table of Contents

Our second core product development program is ALN-AT3, an RNAi therapeutic targeting antithrombin, or AT, a genetically defined target, for the treatment of hemophilia and RBD. ALN-AT3 is a novel therapeutic approach aimed at re-balancing the coagulation cascade and normalizing hemostasis in severe hemophilia A, or HA, and hemophilia B, or HB, patients, including patients with inhibitors against their replacement factor. ALN-AT3 also has potential as a treatment for RBD patients and patients with other bleeding disorders. In July 2013, we presented pre-clinical data showing that ALN-AT3 can normalize thrombin generation and improve hemostasis in HA and HB mice and fully correct thrombin generation in a non-human primate hemophilia inhibitor model, demonstrating efficacy of ALN-AT3 in models of hemophilia. In addition, we presented results of tolerability studies that demonstrate a wide therapeutic index for ALN-AT3 in the hemophilia setting. ALN-AT3 utilizes our GalNAc-siRNA conjugate delivery platform, enabling subcutaneous dose administration with potential for a once-weekly or twice-monthly dosing regimen. In October 2013, we filed a clinical trial application with the U.K. Medicines and Healthcare products Regulatory Agency to initiate a Phase I clinical trial with ALN-AT3. The Phase I clinical trial of ALN-AT3 will be conducted in the United Kingdom as a single- and multi-dose, dose-escalation study consisting of two parts. The first part will be a randomized, single-blind, placebo-controlled, single-dose, dose-escalation study, enrolling up to 24 healthy volunteer subjects. The primary objective of the first part of the study is to evaluate the safety and tolerability of a single dose of subcutaneously administered ALN-AT3. Secondary objectives include assessment of clinical activity as determined by knockdown of circulating AT levels. The second part of the study will be an open-label, multi-dose, dose-escalation study enrolling up to 18 people with moderate to severe HA or HB. The primary objective of this part of the study is to evaluate the safety and tolerability of multiple doses of subcutaneously administered ALN-AT3 in hemophilia subjects. Secondary objectives include assessment of clinical activity as determined by knockdown of circulating AT levels and increase in *ex vivo* thrombin generation. We expect to initiate the Phase I clinical trial during 2014.

We intend to directly commercialize ALN-AT3 in North and South America, Europe and other parts of the world, and we intend to seek a partner for this program in Japan and other Asian territories. In August 2013, we reported that the FDA has provided Orphan Drug Designation to ALN-AT3 as a therapeutic for the treatment of HA and HB.

Our third core development program is ALN-AS1, an RNAi therapeutic targeting aminolevulinate synthase 1, or ALAS-1, for the treatment of porphyria, including AIP. AIP is an ultra-rare autosomal dominant disease caused by loss of function mutations in porphobilinogen deaminase, or PBGD, an enzyme in the heme biosynthesis pathway. ALN-AS1 is a GalNAc conjugate siRNA administered subcutaneously. Inhibition of ALAS-1 is known to reduce the accumulation of heme precursors that cause the clinical manifestations of AIP. ALN-AS1 has the potential to be a therapy for the treatment of acute porphyria attacks, as well as a prophylactic approach for the prevention of recurrent attacks. In October 2013, we announced that we have identified a development candidate for advancement and presented data from pre-clinical models of the human disease showing that multi-dose administration of a GalNAc-siRNA targeting ALAS-1 can completely block the abnormal production of toxic intermediates of the heme biosynthesis pathway that cause the symptoms and disease pathology of AIP. We now plan to initiate IND-enabling studies, with the goal of advancing ALN-AS1 into the clinic. We intend to directly commercialize ALN-AS1 in North and South America, Europe and other parts of the world, and we intend to seek a partner for this program in Japan and other Asian territories.

In addition, we are developing ALN-CC5, an RNAi therapeutic targeting the complement component C5 for the treatment of complement-mediated diseases; ALN-TMP, an RNAi therapeutic targeting transmembrane protease, serine 6, or Tmprss6, for the treatment of beta-thalassemia and iron-overload disorders, and ALN-AAT, an RNAi therapeutic targeting the mutant Z-allele AAT deficiency for the treatment of AAT deficiency-associated liver disease, amongst other programs.

We are also developing ALN-PCS for the treatment of 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, also referred to as bad cholesterol. In February 2013, we and MDCO entered into a license and collaboration agreement pursuant to which we granted to MDCO an exclusive, worldwide license to develop, manufacture and commercialize RNAi therapeutics targeting PCSK9, including ALN-PCS02 and ALN-PCSsc, for the treatment of hypercholesterolemia and other human diseases. See Note 2 to our condensed consolidated financial statements included in this Quarterly Report on Form 10-Q for a more detailed description of the MDCO agreement.

In April 2012, we reported clinical data from our Phase I clinical trial of ALN-PCS02. ALN-PCS02 employs the same LNP formulation used for patisiran. The Phase I clinical trial was conducted in the United Kingdom as a randomized, single-blind, placebo-controlled, single-ascending dose study in healthy volunteer subjects with elevated baseline LDL-c (greater than 116mg/dL). The primary objective of the clinical trial was to evaluate the safety and tolerability of a single dose of ALN-PCS02. Secondary objectives included assessment of pharmacodynamic effects of the drug on plasma PCSK9 protein levels and evaluation of clinical

Table of Contents

efficacy as measured by LDL-c levels. The clinical trial was performed in the absence of statins or other lipid lowering therapy. A total of 32 subjects were enrolled into six sequential dose cohorts ranging from 0.015 to 0.400 mg/kg in a three-to-one randomization of drug to placebo.

In this clinical trial, as reported in April 2012, administration of ALN-PCS02 resulted in rapid, dose-dependent and durable reductions in LDL-c of up to 50% relative to baseline and placebo, with a statistically significant mean reduction of 41% ($p < 0.01$) at the 0.400 mg/kg dose level. In addition, ALN-PCS administration resulted in rapid, dose-dependent and durable knockdown of PCSK9 protein levels in plasma with a maximal 84% reduction relative to baseline and placebo, with a statistically significant mean reduction of 68% in the highest dose group of 0.400 mg/kg ($p < 0.0001$). There was also a dose-dependent increase in the proportion of subjects who achieved target levels of LDL-c of less than 100 mg/dL ($p < 0.05$). ALN-PCS02 was found to be safe and well tolerated in this study and there were no serious adverse events related to study drug administration. There were no drug-related discontinuations and no liver enzyme elevations. A mild, transient rash, observed in 16 subjects, including four who received placebo, is believed to be related to steroid pre-medication provided to subjects receiving both ALN-PCS, as well as those receiving placebo. There were no significant changes compared to baseline in levels of high-density lipoprotein, or HDL, also referred to as good cholesterol, consistent with the phenotype observed in human PCSK9 loss-of-function mutations.

We are also developing a GalNAc-siRNA conjugate targeting PCSK9 that enables subcutaneous dose administration. In October 2013, we and MDCO announced that we have identified a lead development candidate for the collaboration, ALN-PCSSc, that is a subcutaneously administered RNAi therapeutic. Specifically, non-human primate studies performed in the absence of concomitant statin therapy showed that this new development candidate leads to an up to 90% PCSK9 knockdown and an up to 68% lowering of LDL cholesterol in the absence of statins. Pre-clinical durability data support the potential for every-two-weeks dosing, with possible every-four-weeks dosing.

As noted above, 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. We have two partner-based programs in clinical development, ALN-RSV for the treatment of RSV and ALN-VSP for the treatment of liver cancers.

We have a collaboration with Kyowa Hakko Kirin for the development and commercialization of RNAi products for the treatment of RSV in Asia. We also had an agreement with Cubist, pursuant to which Cubist had the right to opt into collaborating with us on ALN-RSV01, subject to certain conditions. In February 2013, Cubist notified us that it would not exercise its opt-in right for ALN-RSV01. In light of this determination, we and Cubist mutually agreed to terminate our license and collaboration agreement. As a result of the termination, the parties have no further rights and obligations under the license and collaboration agreement, notwithstanding anything to the contrary in the agreement. During 2012, we met with the FDA and European regulatory authorities regarding the results of the ALN-RSV01 Phase IIb clinical trial and obtained preliminary guidance on the design of a potential Phase III clinical trial. We intend to seek another partner to advance the ALN-RSV01 program into a Phase III clinical trial and intend to finalize plans with the regulatory authorities and a new partner, if and when identified.

In July 2012, we formed a strategic collaboration with Ascleitis, a privately held US-China joint venture pharmaceutical company, for the development of ALN-VSP. Under the agreement, we have granted Ascleitis exclusive rights to develop and commercialize ALN-VSP in China, including Hong Kong, Macau and Taiwan. We retain all rights to develop and commercialize ALN-VSP in the rest of the world. We may use the data generated in China by Ascleitis under this strategic collaboration for development of ALN-VSP in the rest of the world and Ascleitis may potentially receive sublicense payments based on any such future partnerships. We plan to partner our ALN-VSP program prior to initiating a Phase II clinical trial outside of the Ascleitis territory.

In addition to ALN-RSV and ALN-VSP, we are also supporting the development of ALN-HTT, a novel drug-device product incorporating an RNAi therapeutic candidate targeting the huntingtin gene, delivered using an implantable infusion device, for the treatment of HD, in collaboration with Medtronic. ALN-HTT is currently in pre-clinical development.

In addition to our core development efforts and our additional partner-based programs, we are conducting research activities to discover novel RNAi therapeutic product candidates that we can develop ourselves or partner with third parties with a focus on genetically defined targets and diseases.

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;

Table of Contents

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;

limits on our ability to research, develop, or manufacture our product candidates as a result of contractual obligations to third parties or intellectual property held by third parties;

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 development 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.

Strategic Alliances

A significant component of our business plan is to enter into strategic alliances and collaborations with leading pharmaceutical and life sciences 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. We expect our InterfeRx and research product licenses to generate modest near-term revenues that we can re-invest in the development of our proprietary RNAi therapeutics pipeline. At September 30, 2013, we had granted such licenses, on both an exclusive and non-exclusive basis, to approximately 20 companies.

Since delivery of RNAi therapeutics remains an important 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 Arrowhead, the Massachusetts Institute of Technology, or MIT, The University of

Table of Contents

British Columbia, or UBC, and Acuitas, 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, and Whitehead Institute for Biomedical Research, or Whitehead, as well as a number of other entities, to obtain rights to intellectual property in the field of RNAi. Finally, we have sought, and may seek in the future, funding for the development of our proprietary RNAi therapeutics pipeline from the government and foundations.

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 we refer 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. We have formed several collaborations around our Alnylam Biotherapeutics initiative with leading biotechnology and pharmaceutical companies and may seek additional collaborations with established biologic manufacturers, selling licenses, products and services.

VaxiRNA

We are also applying RNAi technology to improve the manufacturing processes for vaccines in an effort called VaxiRNA. The VaxiRNA platform stems from work we have performed as part of our Alnylam Biotherapeutics efforts. With VaxiRNA, we are using siRNAs that silence specific genes in vaccine production systems, such as cells or chicken eggs, which limit or prevent the efficient growth of viruses used in the manufacture of vaccine products. New innovations in vaccine manufacturing are needed to enable the scale and speed of global immunization for a number of pathogens. In October 2011, we formed a VaxiRNA collaboration with GSK for influenza vaccine production. Under the terms of the agreement, GSK has agreed to provide research funding and certain success-based milestone payments to us. If successfully applied in the manufacture of commercial product, we will also have the right to receive payments on unit product sales, if any. In addition, GSK has obtained an option for VaxiRNA applications toward two additional vaccine products. In 2012, we received a \$3.2 million development milestone payment from GSK under this agreement related to progress in our collaboration.

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. Regulus operates 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 our employees or Isis employees have not been eligible to receive options to purchase Regulus common stock. In October 2012, Regulus completed an underwritten initial public offering, raising \$50.9 million in gross proceeds, including proceeds from the exercise by the underwriters of their over-allotment option. In July 2013, Regulus completed an additional underwritten public offering, raising an additional \$49.2 million in gross proceeds, including proceeds from the exercise of the over-allotment option. Currently, we own approximately 15% of Regulus outstanding common stock.

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. More than 500 microRNAs have been identified to date in humans, each of which is believed to interact with a specific set of genes

Table of Contents

that control key aspects of cell biology. 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 oncology, fibrosis, hepatitis C virus and metabolic diseases.

Regulus has entered into a number of strategic alliances with leading pharmaceutical companies, including GSK, sanofi-aventis, Biogen Idec and AstraZeneca. Each of Alnylam and Isis is entitled to receive specified sublicense income in connection with certain collaborative agreements entered into by Regulus, as well as royalties on net sales, if any, of certain products developed by Regulus or its collaborators, in each case subject to the terms and conditions of the license and collaboration agreement among Regulus, Isis and Alnylam.

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 portfolio 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 portfolio have allowed us to form alliances with leading companies, including Isis, Medtronic, Novartis, Biogen, Roche/Arrowhead, Takeda, Kyowa Hakko Kirin, Cubist, Ascleptis, Monsanto, Genzyme and MDCO, as well as enter into 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

There have been no significant changes to our critical accounting policies since the beginning of this fiscal year. Our critical accounting policies are described in the Management'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, 2012, which we filed with the SEC on February 19, 2013.

Results of Operations

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

	Three Months Ended September 30, 2013		Nine Months Ended September 30, 2013	
	2013	2012	2013	2012
Net revenues	\$ 8,991	\$ 16,759	\$ 36,320	\$ 58,230
Operating expenses	41,225	34,906	99,670	99,337
Loss from operations	(32,234)	(18,147)	(63,350)	(41,107)
Net loss	\$ (29,686)	\$ (19,502)	\$ (56,868)	\$ (43,826)

Table of Contents***Net Revenues from Research Collaborators***

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2013	2012	2013	2012
Takeda	\$ 5,494	\$ 5,494	\$ 16,481	\$ 16,481
Monsanto	1,410	519	4,230	519
The Medicines Company	1,253		3,343	
Cubist		694	9,721	2,084
Roche/Arrowhead		9,330		37,318
Other	834	722	2,545	1,828
Total net revenues from research collaborators	\$ 8,991	\$ 16,759	\$ 36,320	\$ 58,230

Net revenues from research collaborators decreased during the three and nine months ended September 30, 2013 as compared to the three and nine months ended September 30, 2012 due primarily to the completion of our remaining performance obligations under the Roche/Arrowhead alliance in August 2012. For the nine month periods, this decrease was partially offset by recognition of the remaining deferred revenue under the Cubist agreement of \$9.7 million due to the termination of the Cubist agreement in February 2013 and the end of our performance obligations thereunder. In addition, the decrease in each of the three- and nine-month periods was partially offset by revenues recorded under our agreements with Monsanto and MDCO. For the fourth quarter of 2013, we expect net revenues from research collaborators to remain consistent with the amount recorded for the third quarter of 2013.

We also had \$125.3 million of deferred revenue at September 30, 2013, which consists of payments we have received from collaborators in prior periods, primarily Takeda, Kyowa Hakko Kirin, Monsanto, Genzyme and MDCO, 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 Takeda, Monsanto and MDCO, and other strategic alliances, as well as new collaborations and licensing activities.

Operating expenses

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

	Three Months Ended September 30, 2013	% of Total Operating Expenses	Three Months Ended September 30, 2012	% of Total Operating Expenses	Increase (Decrease)	
	\$		\$		\$	%
Research and development	\$ 34,457	84%	\$ 22,094	63%	\$ 12,363	56%

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

General and administrative	6,768	16%	12,812	37%	(6,044)	(47)%
Total operating expenses	\$ 41,225	100%	\$ 34,906	100%	\$ 6,319	18%

	Nine Months Ended September 30, 2013	% of Total Operating Expenses	Nine Months Ended September 30, 2012	% of Total Operating Expenses	Increase (Decrease)	
					\$	%
Research and development	\$ 80,851	81%	\$ 64,891	65%	\$ 15,960	25%
General and administrative	18,819	19%	34,446	35%	(15,627)	(45)%
Total operating expenses	\$ 99,670	100%	\$ 99,337	100%	\$ 333	*

* Indicates less than 1%

Table of Contents

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

	Three Months Ended September 30, 2013	% of Expense Category	Three Months Ended September 30, 2012	% of Expense Category	Increase (Decrease)	
					\$	%
Research and development						
Clinical trial and manufacturing	\$ 12,198	35%	\$ 3,946	18%	\$ 8,252	209%
Stock-based compensation	6,805	20%	2,271	10%	4,534	200%
Compensation and related	6,226	18%	5,387	24%	839	16%
Facilities-related	3,755	11%	3,075	14%	680	22%
External services	3,399	10%	3,860	18%	(461)	(12)%
Lab supplies and materials	1,154	3%	1,125	5%	29	3%
License fees	222	1%	1,813	8%	(1,591)	(88)%
Other	698	2%	617	3%	81	13%
Total research and development expenses	\$ 34,457	100%	\$ 22,094	100%	\$ 12,363	56%

Research and development expenses increased during the three months ended September 30, 2013 as compared to the three months ended September 30, 2012 due primarily to higher clinical trial and manufacturing costs related to our patisiran (ALN-TTR02), ALN-TTRsc and ALN-AT3 programs. In addition, stock-based compensation expense increased during the three months ended September 30, 2013 as compared to the three months ended September 30, 2012 due primarily to an increase in the Black-Scholes value and vesting of stock options granted in the third quarter of 2013. Partially offsetting these increases were license fees due to certain entities related to our drug delivery-related and platform technologies, that were expensed in 2012.

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 and optimize drug delivery-related technologies. For the fourth quarter of 2013, we expect that research and development expenses will decrease slightly due to a decrease in stock-based compensation expense expected in the fourth quarter of 2013 as compared to the third quarter of 2013.

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 not yet in late-stage clinical development. However, our collaboration agreements contain cost-sharing arrangements pursuant to which certain costs incurred under the project are reimbursed by the counterparty to such agreement. 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.

	Nine Months Ended September 30, 2013		Nine Months Ended September 30, 2012		Increase (Decrease)	
		% of Expense Category		% of Expense Category	\$	%
Research and development						
Clinical trial and manufacturing	\$ 21,392	26%	\$ 10,386	16%	\$ 11,006	106%
Compensation and related	18,227	23%	15,731	24%	2,496	16%
External services	12,390	15%	10,150	16%	2,240	22%
Stock-based compensation	11,092	14%	6,356	10%	4,736	75%
Facilities-related	10,622	13%	9,572	15%	1,050	11%
Lab supplies and materials	4,025	5%	3,377	5%	648	19%
License fees	810	1%	4,431	7%	(3,621)	(82)%
Restructuring			2,832	4%	(2,832)	
Other	2,293	3%	2,056	3%	237	12%
Total research and development expenses						
	\$ 80,851	100%	\$ 64,891	100%	\$ 15,960	25%

Table of Contents

Research and development expenses increased during the nine months ended September 30, 2013 as compared to the nine months ended September 30, 2012 due primarily to higher clinical trial and manufacturing costs related to our patisiran, ALN-TTRsc and ALN-AT3 programs. In addition, external services expenses increased due primarily to higher pre-clinical expenses for our patisiran and ALN-AT3 programs which we advanced further in the clinic. Lab supplies and materials and compensation and related expenses also increased due primarily to the increase in workforce during the year. Stock-based compensation increased during the nine months ended September 30, 2013 as compared to the nine months ended September 30, 2012 due primarily to an increase in the Black-Scholes value and vesting of stock options granted in the third quarter of 2013. Partially offsetting these increases was a one-time charge related to our 2012 restructuring, including employee severance, benefits and other related costs, as well as license fees due to certain entities related to our drug delivery-related and platform technologies that were expensed in 2012.

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

	Three Months Ended September 30, 2013		Three Months Ended September 30, 2012		Increase (Decrease)	
		% of Expense Category		% of Expense Category	\$	%
General and administrative						
Stock-based compensation	\$ 2,040	30%	\$ 1,115	9%	\$ 925	83%
Consulting and professional services	1,854	27%	8,930	70%	(7,076)	(79)%
Compensation and related	1,769	26%	1,636	13%	133	8%
Facilities-related	303	5%	445	3%	(142)	(32)%
Other	802	12%	686	5%	116	17%
Total general and administrative expenses	\$ 6,768	100%	\$ 12,812	100%	\$ (6,044)	(47)%

General and administrative expenses decreased significantly during the three months ended September 30, 2013 as compared to the three months ended September 30, 2012 due primarily to a decrease in consulting and professional services related to business activities, primarily legal activities related to litigation with Tekmira that was resolved in November 2012. For the fourth quarter of 2013, we expect that general and administrative expenses will remain consistent as compared to the third quarter of 2013.

	Nine Months Ended September 30, 2013		Nine Months Ended September 30, 2012		Increase (Decrease)	
		% of Expense Category		% of Expense Category	\$	%
General and administrative						
Consulting and professional services	\$ 6,363	34%	\$ 22,199	64%	\$ (15,836)	(71)%
Compensation and related	5,146	27%	4,909	14%	237	5%

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

Stock-based compensation	4,205	22%	3,281	9%	924	28%
Restructuring			894	3%	(894)	
Facilities-related	1,126	6%	1,241	4%	(115)	(9)%
Other	1,979	11%	1,922	6%	57	3%

Total general and administrative

expenses	\$ 18,819	100%	\$ 34,446	100%	\$ (15,627)	(45)%
-----------------	-----------	------	-----------	------	-------------	-------

The decrease in general and administrative expenses during the nine months ended September 30, 2013 as compared to the nine months ended September 30, 2012 was due primarily to a decrease in consulting and professional services expenses related to business activities, primarily legal activities related to litigation with Tekmira that was resolved in November 2012. Also included in the nine months ended September 30, 2012 is a one-time charge related to our January 2012 strategic corporate restructuring, including employee severance, benefits and other related costs.

Other income (expense)

We incurred zero in equity in loss of joint venture (Regulus Therapeutics Inc.) for the three and nine months ended September 30, 2013, respectively, as compared to \$1.6 million and \$3.6 million for the three and nine months ended September 30, 2012, respectively, related to our share of the net losses incurred by Regulus. In October 2012, Regulus completed an initial public offering, resulting in our ownership percentage decreasing from approximately 44% to 17% of Regulus' outstanding common stock.

Table of Contents

In July 2013, Regulus completed an additional underwritten public offering, further reducing our ownership percentage to approximately 15%. Based upon our ownership percentage of approximately 15%, as well as qualitative factors, we do not believe that we have the ability to exercise significant influence over the operating decisions and financial policies of Regulus and therefore have discontinued the equity method of accounting for Regulus. Accordingly, beginning in October 2012, we have accounted for our investment in Regulus as an available-for-sale marketable security.

Interest income was \$0.3 million for the three months ended September 30, 2013 and 2012. Interest income was \$0.8 million for the nine months ended September 30, 2013 and 2012.

Our benefit from income taxes was \$2.3 million and \$5.7 million for the three and nine months ended September 30, 2013, respectively, as compared to zero for the three and nine months ended September 30, 2012. The increase was due to our recognition of corresponding income tax benefit associated with the increase in the value of our investment in Regulus that we carried at fair market value during the same respective period.

Liquidity and Capital Resources

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

	Nine Months Ended September 30,	
	2013	2012
Net loss	\$ (56,868)	\$ (43,826)
Adjustments to reconcile net loss to net cash used in operating activities	17,534	20,421
Changes in operating assets and liabilities	(6,954)	(23,292)
Net cash used in operating activities	(46,288)	(46,697)
Net cash used in investing activities	(186,553)	(40,139)
Net cash provided by financing activities	193,276	92,446
Net (decrease) increase in cash and cash equivalents	(39,565)	5,610
Cash and cash equivalents, beginning of period	51,405	70,228
Cash and cash equivalents, end of period	\$ 11,840	\$ 75,838

Since we commenced operations in 2002, we have generated significant losses. At September 30, 2013, we had an accumulated deficit of \$563.9 million. At September 30, 2013, we had cash, cash equivalents and fixed income marketable securities of \$367.1 million, compared to cash, cash equivalents and fixed income marketable securities of \$226.2 million at December 31, 2012. Included in our December 31, 2012 cash, cash equivalents and fixed income marketable securities are the proceeds from our sale, in February 2012, of an aggregate of 8,625,000 shares of our common stock through an underwritten public offering at a price to the public of \$10.75 per share. As a result of this offering, we received aggregate net proceeds of approximately \$86.8 million, after deducting underwriting discounts and commissions and other estimated offering expenses of approximately \$5.9 million. Included in our September 30, 2013 cash, cash equivalents and fixed income marketable securities are the proceeds from our sale, in January 2013, of an aggregate of 9,200,000 shares of our common stock through an underwritten public offering at a price to the public of \$20.13 per share. As a result of this offering, we received aggregate net proceeds of approximately \$173.6

million, after deducting underwriting discounts and commissions and other estimated offering expenses of approximately \$11.6 million. We intend to use the proceeds from these offerings for general corporate purposes, ultimately focused on advancing our clinical pipeline, in particular our patisiran, ALN-TTRsc, ALN-AT3 and ALN-AS1 programs, as well as for potential acquisitions of new businesses, technologies or products, working capital, capital expenditures, and general and administrative expenses.

We invest primarily in cash equivalents, U.S. government obligations, high-grade corporate notes and commercial paper. Our investment objectives are, primarily, to assure liquidity and preservation of capital and, secondarily, to obtain investment income. All of our investments in debt securities are recorded at fair value and are available-for-sale. Fair value is determined based on quoted market prices and models using observable data inputs. We have not recorded any impairment charges related to our fixed income marketable securities at September 30, 2013.

Operating activities

We have required significant amounts of cash to fund our operating activities as a result of net losses since our inception. For the nine months ended September 30, 2013, net cash used in operating activities of \$46.3 million was due primarily to our net loss. For the nine months ended September 30, 2012, net cash used in operating activities of \$46.7 million was due primarily to our

Table of Contents

net loss and a decrease in deferred revenue of \$24.7 million. 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, 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 nine months ended September 30, 2013, net cash used in investing activities of \$186.6 million was due primarily to net purchases of fixed income marketable securities. For the nine months ended September 30, 2012, net cash used in investing activities of \$40.1 million resulted primarily from net purchases of fixed income marketable securities.

Financing activities

For the nine months ended September 30, 2013, net cash provided by financing activities of \$193.3 million was due primarily to proceeds of \$173.6 million received from our January 2013 underwritten public offering, as well as proceeds of \$19.8 million from the issuance of common stock in connection with stock option exercises. For the nine months ended September 30, 2012, net cash provided by financing activities of \$92.4 million was due primarily to proceeds received from our February 2012 underwritten public offering, 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 and optimization 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, together with the cash we expect to generate under our current alliances, will be sufficient to fund our planned operations through at least the end of 2016. For 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 December 2012, we filed an automatically effective shelf registration statement with the SEC for an indeterminate number of shares. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any additional financing may further 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. As a condition to providing additional funds to us, future investors may also 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;

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 success of any proposed financing efforts;

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;

our ability to manufacture, or contract with third-parties for the manufacture of, our product candidates for clinical testing and commercial sale;

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

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, 2012. There have been no material changes in our contractual obligations and commitments since December 31, 2012. However, in March 2013, sanofi-aventis U.S. Inc., or sanofi, notified us that it was exercising its right to terminate its sublease agreement with us as of December 31, 2013. As a result of this early termination, sanofi will be required to pay us a termination fee. We do not believe that the termination of the sanofi sublease is material to our business.

Recent Accounting Pronouncements

In February 2013, the Financial Accounting Standards Board, or FASB, issued amendments to the accounting guidance for presentation of comprehensive income to improve the reporting of reclassifications out of accumulated other comprehensive income. The amendments did not change the current requirements for reporting net income or other comprehensive income, but require an entity to provide information about the amounts reclassified out of accumulated other comprehensive income by component. In addition, an entity is now required to present, either on

the face of the statement where the net income is presented or in the notes, significant amounts reclassified out of accumulated other comprehensive income by the respective line items of net income but only if the amount reclassified is required accordance with accounting principles generally accepted in the United States of America, or GAAP, to be reclassified to net income in its entirety in the same reporting period. For other amounts that are not required under GAAP to be reclassified in their entirety to net income, an entity is required to cross-reference to other disclosures required under GAAP that provide additional detail about these amounts. For public companies, these amendments were effective prospectively for reporting periods beginning after December 15, 2012. We adopted this guidance on January 1, 2013. Other than a change in presentation, the adoption of this guidance did not have a material impact to our condensed consolidated financial statements.

In July 2013, the FASB issued new accounting guidance specific to income taxes. The new guidance requires an entity to present an unrecognized tax benefit and a net operating loss carryforward, a similar tax loss, or a tax credit carryforward on a net basis as part of a deferred tax asset, unless the unrecognized tax benefit is not available to reduce the deferred tax asset component or would not be utilized for that purpose, then a liability would be recognized. The updated accounting guidance is effective for fiscal years beginning after December 15, 2013. We do not expect the adoption of this guidance to have a material impact on our condensed consolidated financial statements.

Table of Contents

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

As part of our investment portfolio, we own financial instruments that are sensitive to market risks. The investment portfolio is used to preserve our capital until it is required to fund operations, including our research and development activities. Our fixed income marketable securities consist of U.S. government obligations, high-grade corporate notes and commercial paper. All of our investments in debt securities are classified as available-for-sale and are recorded at fair value. Our available-for-sale investments in debt securities are sensitive to changes in interest rates and changes in the credit ratings of the issuers. Interest rate changes would result in a change in the net fair value of these financial instruments due to the difference between the market interest rate and the market interest rate at the date of purchase of the financial instrument. If market interest rates were to increase immediately and uniformly by 50 basis points, or one-half of a percentage point, from levels at September 30, 2013, the net fair value of our interest-sensitive financial instruments would have resulted in a hypothetical decline of \$1.7 million. We currently do not seek to hedge this exposure to fluctuations in interest rates. 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 September 30, 2013.

ITEM 4. CONTROLS AND PROCEDURES.

Our management, with the participation of our chief executive officer (principal executive officer) and vice president of finance and treasurer (principal financial officer), evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2013. 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 controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, as appropriate to allow timely decisions regarding required disclosure. Management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of September 30, 2013, 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(f) and 15d-15(f) under the Exchange Act) occurred during the three months ended September 30, 2013 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Table of Contents

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS.

University of Utah Litigation

On March 22, 2011, The University of Utah, or Utah, filed a civil complaint in the United States District Court for the District of Massachusetts against us, Max Planck Gesellschaft Zur Foerderung Der Wissenschaften e.V. and Max Planck Innovation, together, Max Planck, Whitehead, MIT and the University of Massachusetts, or UMass, claiming a professor at Utah is the sole inventor or, in the alternative, a joint inventor, of the Tuschl patents. Utah did not serve the original complaint on us or the other defendants. On July 6, 2011, Utah 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. Utah is seeking changes to the inventorship of the Tuschl patents, unspecified damages and other relief. On October 31, 2011, we, Max Planck, Whitehead, MIT and UMass filed a motion to dismiss. Also on October 31, 2011, UMass filed a motion to dismiss on separate grounds, which we, Max Planck, Whitehead and MIT joined. On December 31, 2011, Utah filed a second amended complaint dropping UMass as a defendant and adding as defendants several UMass officials. In June 2012, the Court denied both motions to dismiss. We, Max Planck, Whitehead, MIT and UMass filed an appeal of the Court's ruling on the motion to dismiss for lack of jurisdiction and a motion requesting that the Court stay the case pending the outcome of the appeal. In July 2012, the Court stayed discovery in the case pending the outcome of the defendants' appeal. Oral arguments in the appeal were heard in early March 2013 in the United States Court of Appeals for the Federal Circuit, or CAFC. In August 2013, the CAFC affirmed the lower Court's ruling, in a split decision. We believe the majority made an error in law when affirming the lower Court's decision, and in September 2013, we filed a petition with the CAFC for rehearing or rehearing *en banc*. In October 2013, the CAFC invited Utah to file an answer to the petition. We are awaiting a decision on the petition.

Although we believe we have meritorious defenses and intend to vigorously defend ourselves in this matter, litigation is subject to inherent uncertainty and a court could ultimately rule against us. 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 other activities. We have not recorded an estimate of the possible loss associated with this legal proceeding due to the uncertainties related to both the likelihood and the amount of any possible loss or range of loss.

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 are in early-stage clinical development, there is limited information about our ability to successfully overcome many of the risks and uncertainties encountered by companies in the biopharmaceutical industry.

As a company in the early stages of clinical development, 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.

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.

Table of Contents

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 September 30, 2013, we had an accumulated deficit of \$563.9 million. To date, we have not developed any products nor generated any revenues from the sale of products. Further, we do not expect to generate any such revenues in the foreseeable future. We expect to continue to incur annual net operating losses over the next several years and will require substantial resources over the next several years as we expand our efforts to discover, develop and commercialize RNAi therapeutics. We anticipate that the majority of any revenues we generate over the next several years will be from alliances with pharmaceutical and biotechnology companies, but cannot be certain that we will be able to secure or maintain these alliances, or meet the obligations or achieve any milestones that we may be required to meet or achieve to receive payments. We anticipate that revenues 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, develop additional product candidates 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 our product candidates, and to manufacture and market any products that are approved for commercial sale. Because we cannot be certain of the length of time or activities associated with successful development of our product candidates, 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;

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

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

the success of any proposed financing efforts;

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;

our ability to manufacture, or contract with third-parties for the manufacture of, our product candidates for clinical testing and commercial sale;

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

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;

Table of Contents

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. 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 GAAP. 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.

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

At September 30, 2013, we had \$367.1 million in cash, cash equivalents and fixed income marketable securities. We historically have invested these amounts in corporate bonds, commercial paper, securities issued by the U.S. government, certificates of deposit and money market funds meeting the criteria of our investment policy, which is focused on the preservation of our capital. These investments are subject to general credit, liquidity, market and interest rate risks, 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. The 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. In November 2010, Roche announced the discontinuation of certain activities in research and early development, including their RNAi research efforts. In October 2011, Arrowhead announced its acquisition of RNA therapeutics assets from Roche, including our license and collaboration agreement with Roche. As a result of the assignment, Arrowhead now has all of the rights and obligations of Roche under that agreement. The license is limited to four therapeutic areas and may be expanded to include additional therapeutic areas, upon payment to us by Arrowhead 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 Arrowhead, 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. Our receipt of milestone payments under this agreement is dependent upon Arrowhead's ability to successfully develop and commercialize RNAi therapeutic products.

Table of Contents

In May 2008, we entered into a similar license and collaboration agreement with Takeda, which is limited to two therapeutic areas, and which may be expanded to include additional therapeutic areas, 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 milestone payments, totaling up to \$171.0 million per product, together with royalty payments based on worldwide annual net sales, if any.

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 any.

If Takeda, Novartis or Arrowhead fails to successfully develop products using our technology, we may not receive any milestone or royalty payments under our agreements with them. In addition, we have the option under the Takeda agreement, exercisable until the start of Phase III development, to opt-in under a 50-50 profit sharing agreement to the development and commercialization in the United States of up to four Takeda licensed products, and would be entitled to opt-in rights for two additional products for each additional field expansion, if any, elected by Takeda under the collaboration agreement. If Takeda fails to successfully develop products, we may not realize any economic benefit from these opt-in rights. Finally, Takeda could become a competitor of ours in the development of RNAi-based drugs targeting the same diseases that we choose to target. Takeda has 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 terms favorable to us, 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 such alliances in the future. Specifically, we intend to focus on developing and commercializing patisiran (ALN-TTR02), ALN-TTRsc, ALN-AT3, ALN-AS1 and ALN-CC5 on our own in North and South America, Europe and other parts of the world, and have sought, or may seek, alliances for development and commercialization of these product candidates in Japan and other Asian territories. In February 2013, we entered into a global alliance with MDCO to advance our ALN-PCS program. We may enter into global alliances to advance certain other programs in the future. 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. In addition, we have agreements with MIT, Tekmira, UBC and Acuitas, and Arrowhead, among others, pursuant to which we have access to certain existing delivery technologies and/or are developing additional delivery capabilities. Under certain of our other alliances, we also may expect our collaborators to develop, market and/or 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 (i) Ascleitis for development and commercialization of any RNAi products for the treatment of liver cancer in China and certain other

territories, (ii) Genzyme for the development and commercialization of ALN-TTR in Japan and the Asia-Pacific region, and (iii) MDCO for the late stage development and commercialization of ALN-PCS worldwide. If Ascleitis, Genzyme and/or MDCO are not successful in their commercialization efforts, our future revenues from RNAi therapeutics for these indications may be adversely affected.

We may not be successful in entering into such alliances on terms favorable to us due to various factors, including our ability to successfully demonstrate proof of concept for our technology in humans, our ability to demonstrate the safety and efficacy of our specific drug candidates, our ability to manufacture or have manufactured RNAi therapeutics, the strength of our intellectual property and/or concerns around challenges to 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, challenges are raised as to the validity or scope of our intellectual property or sales of an approved drug are lower than we expected. In the case of the Monsanto agreement, if we cease to own or otherwise exclusively control certain licensed patent rights in the agriculture field, resulting in the loss of exclusivity with respect to Monsanto's rights to such patent rights, and such loss of exclusivity has a material adverse effect on the licensed products (as defined in the agreement), we would be required to pay Monsanto up to \$5.0 million in liquidated damages, and Monsanto's royalty obligations to us would be reduced or, under certain circumstances, terminated.

Table of Contents

Furthermore, any delay in entering into collaboration agreements would likely either delay the development and commercialization of certain of our product candidates and reduce their competitiveness even if they reach the market, or prevent the development of certain product candidates. 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, Medtronic and MDCO. We may not, however, be able to enter into additional collaborations for certain other programs, including ALN-TMP, ALN-VSP or ALN-RSV, 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 one or more of these product candidates, 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 collaboration for a material breach by the other party. For example, our agreement with MDCO relating to the development and commercialization of ALN-PCS worldwide may be terminated by MDCO at any time upon four months' prior written notice. 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 could delay our development of product candidates, result in the need for additional company resources to develop product candidates, make it more difficult for us to attract new collaborators and could adversely affect how we are perceived in the business and financial communities. For example, in March 2011, Tekmira filed a civil complaint against us claiming, among other things, misappropriation of its confidential and proprietary information and trade secrets. As a result of the litigation, which was settled in November 2012, we were required to expend resources and management attention that would otherwise have been engaged in other activities. In addition, in August 2013, we initiated binding arbitration proceedings to resolve a disagreement with Tekmira regarding the achievement by Tekmira of a \$5.0 million milestone payment under our cross-license agreement relating to the manufacture of ALN-VSP clinical trial material for use in China. 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 interests 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.

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 contracted, and we plan to continue to contract with, certain third-parties to provide certain services, including site selection, enrollment, monitoring and data management services.

Table of Contents

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 and timely fulfill their obligations to us, or if the quality and accuracy of our clinical trial data is compromised due to failure by such third-party 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 and/or rely on third parties to manufacture our products.

We have very limited manufacturing experience. Some of our product candidates utilize specialized formulations, such as liposomes or LNP-based formulations, 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. Our internal manufacturing capabilities have been limited to small-scale production of material for use in *in vitro* and *in vivo* experiments that is not required to be produced under current good manufacturing practice, or cGMP, standards. During 2012, we developed cGMP capabilities and processes for the manufacture of patisiran for Phase III clinical trial use and early commercial supply.

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, such as LNPs or conjugates. In some cases, the delivery technology we utilize is highly specialized or proprietary, and for technical and legal reasons, we may have access to only one or a limited number of potential manufacturers for such delivery technology. Failure by manufacturers to properly formulate our siRNAs for delivery could result in unusable product. Furthermore, a breach by such manufacturers of their contractual obligations or a dispute with such manufacturers would cause delays in our discovery and development efforts, as well as additional expense to us. Given the limited number of suppliers for our delivery technology and other materials, we have developed cGMP capabilities and processes for the manufacture of patisiran for Phase III clinical use and early commercial supply, and in the future, we may also develop our own capabilities to manufacture drug substance, including siRNAs and siRNA conjugates for human clinical use. In developing these manufacturing capabilities by building our own manufacturing facility, we have incurred substantial expenditures. Also, we will need to hire and train employees to staff our new facility.

The manufacturing process for any products that we may develop is subject to FDA and foreign regulatory authority approval process and we will need to meet, and 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 have existing, or enter into future, manufacturing arrangements with third parties, we depend, and will depend in the future, 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, or, to the extent we manufacture all or a portion of our product candidates ourselves, our failure to execute on our manufacturing requirements could adversely affect our business in a number of ways, including:

we or our current or future collaborators may not be able to initiate or continue clinical trials of products that are under development;

we or our current or future collaborators 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;

Table of Contents

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

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

If 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 products or product candidates may be unique or proprietary to the original manufacturer and we may have difficulty, or there may be contractual restrictions prohibiting us from, 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 or product candidates.

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, 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 and January 2012 corporate restructurings and workforce reductions, 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.

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

Despite our January 2012 workforce reduction in connection with our strategic corporate restructuring, we expect that as we are increasing the number of product candidates we are developing we will also need to expand our operations. This expected growth may

Table of Contents

place a strain on our administrative and operational infrastructure. As 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, including patisiran in Phase II clinical trials and ALN-TTRsc, ALN-PCS and ALN-VSP in Phase I clinical development. 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-VSP, ALN-PCS, patisiran and ALN-TTRsc 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 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. For example, we may experience difficulty enrolling our clinical trials, including, but not limited to, our clinical trials for patisiran, due to the small population of patients suffering from ATTR and the availability of existing approved treatments, as well as other investigational treatments in development. Although our RNAi therapeutics have been generally safe and well tolerated in our clinical trials to date, 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. In addition, in our ALN-VSP and ALN-TTR01 Phase I clinical trials, we have reported an incidence of acute infusion reactions occurring in 15-20% of patients. These were graded as mild or moderate in severity and readily responded to slowing of the infusion rate; all patients completed dosing without further incident. The frequency of acute infusion reactions in our ALN-PCS and patisiran Phase I clinical trials has been less than three percent. In our ALN-PCS clinical trial, we reported the occurrence of a mild, transient rash that was observed in sixteen subjects, including four who received placebo; the incidence of this finding was the same in both placebo and drug treatment arms. Delays or difficulties in patient enrollment or difficulties retaining trial participants, including as a result of the availability of existing or other investigational treatments or the occurrence of adverse events, can result in increased costs, longer development times or termination of a clinical trial.

Table of Contents

Clinical trials also require the review, oversight and approval of IRBs, which 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;

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.

Table of Contents

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. 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, 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, packaging, advertising and promotion, pricing, 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 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 FDA's standards, especially regarding drug safety, appear to have become more stringent.

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 Strategy, or REMS, plan as part of an NDA or biologics license application, or BLA, 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.

Table of Contents

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 and listing, 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.

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 have recently developed cGMP capabilities and processes for the manufacture of patisiran for Phase III clinical and early commercial use. We may not have the ability to manufacture material for a broader commercial scale in the future. 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. We will not have control over our third-party manufacturers' compliance with applicable rules and regulations. 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;

the prevalence and severity of any adverse side effect associated with our product candidates;

limitations or warnings contained in FDA approved labeling;

Table of Contents

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.

In addition, our estimates regarding the potential market size may be materially different from what we currently expect at the time we commence commercialization, which could result in significant changes in our business plan and may have a material adverse effect on our results of operations and financial condition.

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;

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;

the federal Open Payments regulations under the National Physician Payment Transparency Program have been issued under PPACA and will require that manufacturers of pharmaceutical and biological drugs covered by Medicare, Medicaid, and Children's Health Insurance Programs report all consulting fees, travel reimbursements, research grants, and other payments or gifts with values over \$10 made to physicians and teaching hospitals; 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, healthcare reimbursement or other government programs, including Medicare and Medicaid, any of which could adversely affect 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;

Table of Contents

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.

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 or healthcare providers, 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 or the amounts reimbursed for pharmaceutical products. If the price we are able to charge for any products we develop, or the reimbursement provided for such products, is inadequate in light of our development and other costs, our return on investment could be adversely affected.

We currently expect that any drugs we develop may need to be administered under the supervision of a physician on an outpatient basis. Under currently applicable U.S. law, certain drugs that are not usually self-administered (including injectable drugs) may be eligible for coverage under the Medicare Part B 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; and

they have been approved by the FDA and meet other requirements of the statute.

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

Table of Contents

payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates. Our inability to promptly obtain coverage and adequate 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 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. 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 approval of an application for a follow-on biologic product may not become effective until 12 years after the date on which the reference innovator biologic product was first

licensed by the FDA, with a possible six-month extension for pediatric products. After this exclusivity ends, it will be easier for generic manufacturers to enter the market, which is likely to reduce the pricing for such products and could affect our profitability.

The full effects of the U.S. healthcare reform legislation cannot be known until the new law is fully 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.

Our ability to obtain services, reimbursement or funding from the federal government may be impacted by possible reductions in federal spending.

U.S. federal government agencies currently face potentially significant spending reductions. Under the Budget Control Act of 2011, the failure of Congress to enact deficit reduction measures of at least \$1.2 trillion for the years 2013 through 2021 triggered automatic cuts to most federal programs. These cuts would include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, starting in 2013. Under the American Taxpayer Relief Act of 2012, which was enacted on January 1, 2013, the imposition of these automatic cuts was delayed until March 1, 2013. Certain of these automatic cuts have been implemented. The full impact on our business of these automatic cuts is uncertain.

Table of Contents

If federal spending is reduced, anticipated budgetary shortfalls may also impact the ability of relevant agencies, such as the FDA or NIH to continue to function at current levels. Amounts allocated to federal grants and contracts may be reduced or eliminated. These reductions may also impact the ability of relevant agencies to timely review and approve drug research and development, manufacturing, and marketing activities, which may delay our ability to develop, market and sell any products we may develop.

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 decreased demand for our products, injury to our reputation, costs to defend the related litigation, a diversion of management's time and our resources, substantial monetary awards to trial participants or patients and a decline in our stock price. 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.

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, development and manufacturing 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, development and manufacturing 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 facilities comply with the relevant guidelines of the City of Cambridge, the Commonwealth of Massachusetts and the Occupational Safety and Health Administration of the U.S. Department of Labor. 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.

Table of Contents

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. 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. Moreover, there are periodic discussions in the Congress of the United States and in international jurisdictions about modifying various aspects of patent law. For example, the America Invents Act includes a number of changes to the patent laws of the United States. If any changes to the patent laws 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 Innovation, Tekmira and Arrowhead. 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.

Table of Contents

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 European Patent Office, or EPO, and in other jurisdictions. We expect that additional oppositions will be filed in the EPO and elsewhere, and other challenges will be raised relating to other patents and patent applications in our portfolio. In many cases, the possibility of appeal exists for either us or our opponents, and it may be years before final, unappealable rulings are made with respect to these patents in certain jurisdictions. The timing and outcome of these and other proceedings is uncertain and may adversely affect our business if we are not successful in defending the patentability and scope of our pending and issued patent claims. In addition, third parties may attempt to invalidate our intellectual property rights. Even if our rights are not directly challenged, disputes could lead to the weakening of our intellectual property rights. Our defense against any attempt by third parties to circumvent or invalidate our intellectual property rights could be costly to us, could require significant time and attention of our management and could have a material adverse effect on our business and our ability to successfully compete in the field of RNAi.

There are many issued and pending patents that claim aspects of oligonucleotide chemistry and modifications 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 filed a civil complaint against us alleging, among other things, misappropriation of the plaintiffs confidential and proprietary information and trade secrets. In November 2012, we settled this litigation and restructured our contractual relationship with Tekmira. In connection with this restructuring, we incurred a \$65.0 million charge to operating expenses during the quarter ended December 31, 2012. In addition, during the pendency of the litigation, we incurred significant costs, and the defense of this litigation diverted the attention of our management and other resources that would otherwise have been engaged in other activities.

Furthermore, third parties may challenge the inventorship of our patents or licensed patents. For example, in March 2011, 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 Utah 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, Utah 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. In October 2011, we, Max Planck, Whitehead, MIT and UMass filed a motion to dismiss and UMass filed a motion to dismiss on separate grounds, which we, Max Planck, Whitehead and MIT have joined. In December 2011, Utah filed a second amended complaint dropping UMass as a defendant and adding as defendants several UMass officials. In June 2012, the Court denied both motions to dismiss. We, Max Planck, Whitehead, MIT and UMass filed an appeal of the Court's ruling on the motion to dismiss for lack of jurisdiction and a motion requesting that the Court stay the case pending the outcome of the appeal. In July 2012, the Court stayed discovery in the case pending the outcome of the defendants' appeal. Oral arguments in the appeal were heard in early March 2013 in the United States Court of Appeals for the Federal Circuit, or CAFC. In August 2013, the CAFC affirmed the lower Court's ruling, in a split decision. We believe the majority made an error in law when affirming the lower Court's decision, and in September 2013, we filed a petition with the CAFC for rehearing or rehearing *en banc*. In October 2013, the CAFC invited Utah to file an answer to the petition. We are awaiting a decision on the petition.

We intend to vigorously defend ourselves in this matter, however, litigation is subject to inherent uncertainty and a court could ultimately rule against us.

Table of Contents

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

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

Our current licenses impose, and any future licenses we enter into are likely to impose, various development, commercialization, funding, milestone, royalty, diligence, sublicensing, insurance, patent prosecution and enforcement, and other obligations on us. If we breach any of these obligations, or use the intellectual property licensed to us in an unauthorized manner, we may be required to pay damages and 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. For example, Tekmira has notified us that it believes it has achieved a \$5.0 million milestone payment under our cross-license agreement relating to the manufacture of ALN-VSP clinical trial material for use in China. We have notified Tekmira that we do not believe that the milestone has been achieved under the terms of the cross-license agreement. In August 2013, we initiated binding arbitration proceedings seeking a declaratory judgment that Tekmira has not yet met the conditions of the milestone and is not entitled to payment at this time. If it is determined through arbitration that Tekmira has met the requirements of the milestone, we will have to pay Tekmira the milestone.

Moreover, our licensors may own or control intellectual property that has not been licensed to us and, as a result, we may be subject to claims, regardless of their merit, that we are infringing or otherwise violating the licensor's rights. 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;

Table of Contents

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, hemophilia and RBD, AIP, complement-mediated disorders, beta-thalassemia and iron-overload disorders, AAT deficiency-associated liver disease, hypercholesterolemia, RSV, liver cancers and HD, and have a number of additional discovery programs targeting other diseases. Other available 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:

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., Arrowhead and its subsidiary, Calando Pharmaceuticals, Inc., Tekmira, Quark Pharmaceuticals, Inc., Sylentis S.A.U. 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.

Table of Contents

In addition, as a result of agreements that we have entered into, Arrowhead, as the assignee of 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 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, including one for the treatment of ATTR. The development of antisense drugs is more advanced than that of RNAi therapeutics, and antisense technology may become the preferred technology for drugs that target mRNAs to silence specific genes.

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

Risks Related to Our Common Stock

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

The market price of our common stock has fluctuated 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.

Sales of additional shares of our common stock, including by us or our directors and officers, could 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 our officers and directors, or others, including the issuance of common stock upon exercise of outstanding options or restricted stock, could adversely affect the price of our common stock.

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.

Table of Contents

In addition, our board of directors has adopted a stockholder rights plan, the provisions of which could make it difficult for a potential acquirer of Alnylam to consummate an acquisition transaction. Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. These provisions would apply even if the proposed merger or acquisition could be considered beneficial by some stockholders.

ITEM 6. EXHIBITS.

- 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 the Registrant's Quarterly Report on Form 10-Q for the quarter ended September 30, 2013, formatted in XBRL (Extensible Business Reporting Language): (i) the Condensed Consolidated Balance Sheets, (ii) the Condensed Consolidated Statements of Comprehensive Loss, (iii) the Condensed Consolidated Statements of Cash Flows, and (iv) Notes to Condensed Consolidated Financial Statements.

Table of Contents

SIGNATURES

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

ALNYLAM PHARMACEUTICALS, INC.

Date: November 7, 2013

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

Date: November 7, 2013

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