

ALNYLAM PHARMACEUTICALS, INC.

Form 10-Q

November 04, 2010

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

FORM 10-Q

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

For the quarterly period ended September 30, 2010

OR

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

For the transition period from _____ to _____

Commission File Number 000-50743

ALNYLAM PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Its Charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

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

300 Third Street, Cambridge, MA

02142

(Address of Principal Executive
Offices)

(Zip Code)

(617) 551-8200

(Registrant's Telephone Number, Including Area Code)

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

Indicate by check mark whether the registrant 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

Smaller reporting
company

(Do not check if a 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

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As of October 29, 2010, the registrant had 42,199,840 shares of Common Stock, \$0.01 par value per share, outstanding.

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

	September 30, 2010	December 31, 2009
ASSETS		
Current assets:		
Cash and cash equivalents	\$ 46,881	\$ 137,468
Marketable securities	184,486	143,934
Collaboration receivables	4,881	6,044
Prepaid expenses and other current assets	6,432	4,151
Deferred tax assets	1,943	1,885
Total current assets	244,623	293,482
Marketable securities	140,503	153,914
Property and equipment, net	18,399	18,324
Deferred tax assets, net of current portion	8,570	8,414
Investment in joint venture (Regulus Therapeutics Inc.)	20	6,435
Intangible assets, net	491	622
Total assets	\$ 412,606	\$ 481,191
 LIABILITIES AND STOCKHOLDERS EQUITY		
Current liabilities:		
Accounts payable	\$ 6,561	\$ 12,489
Accrued expenses	10,880	9,833
Income taxes payable	237	5,644
Deferred rent	485	838
Deferred revenue	81,270	81,929
Total current liabilities	99,433	110,733
Deferred rent, net of current portion	2,864	2,609
Deferred revenue, net of current portion	149,666	189,884
Total liabilities	251,963	303,226
Commitments and contingencies (Notes 3, 5 and 6)		
Stockholders equity:		
Preferred stock, \$0.01 par value, 5,000,000 shares authorized and no shares issued and outstanding at September 30, 2010 and December 31, 2009		
Common stock, \$0.01 par value, 125,000,000 shares authorized; 42,160,382 shares issued and outstanding at September 30, 2010; 41,837,427 shares issued and outstanding at December 31, 2009	422	418

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Additional paid-in capital	495,350	476,663
Accumulated other comprehensive income	1,288	716
Accumulated deficit	(336,417)	(299,832)
Total stockholders' equity	160,643	177,965
Total liabilities and stockholders' equity	\$ 412,606	\$ 481,191

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

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

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2010	2009	2010	2009
Net revenues from research collaborators	\$ 27,668	\$ 24,249	\$ 78,849	\$ 73,907
Operating expenses:				
Research and development ⁽¹⁾	27,468	23,219	80,304	87,155
General and administrative ⁽¹⁾	8,928	10,680	30,205	26,794
Total operating expenses	36,396	33,899	110,509	113,949
Loss from operations	(8,728)	(9,650)	(31,660)	(40,042)
Other income (expense):				
Equity in loss of joint venture (Regulus Therapeutics Inc.)	(1,226)	(1,136)	(6,723)	(3,422)
Interest income	602	1,036	1,833	4,542
Other income (expense)	20	(10)	52	144
Total other income (expense)	(604)	(110)	(4,838)	1,264
Loss before income taxes	(9,332)	(9,760)	(36,498)	(38,778)
(Provision for) benefit from income taxes	(298)	552	(87)	(1,021)
Net loss	\$ (9,630)	\$ (9,208)	\$ (36,585)	\$ (39,799)
Net loss per common share basic and diluted	\$ (0.23)	\$ (0.22)	\$ (0.87)	\$ (0.96)
Weighted average common shares used to compute basic and diluted net loss per common share	42,123	41,708	41,989	41,543
Comprehensive loss:				
Net loss	\$ (9,630)	\$ (9,208)	\$ (36,585)	\$ (39,799)
Foreign currency translation		(4)	(29)	(117)
Unrealized gain on marketable securities	2	272	601	820
Comprehensive loss	\$ (9,628)	\$ (8,940)	\$ (36,013)	\$ (39,096)

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

Research and development	\$ 2,725	\$ 3,128	\$ 9,200	\$ 9,410
General and administrative	1,786	2,110	5,706	6,377

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

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

	Nine Months Ended September	
	30,	
	2010	2009
Cash flows from operating activities:		
Net loss	\$ (36,585)	\$ (39,799)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:		
Depreciation and amortization	3,650	4,856
Deferred income taxes	(133)	31
Non-cash stock-based compensation	14,906	15,787
Charge for 401(k) company stock match	402	365
Equity in loss of joint venture (Regulus Therapeutics Inc.)	6,723	3,422
Changes in operating assets and liabilities:		
Collaboration receivables	1,163	(834)
Prepaid expenses and other assets	(2,281)	(499)
Accounts payable	(5,928)	5,838
Income taxes payable	(5,546)	(4,794)
Accrued expenses and other	553	(1,761)
Deferred revenue	(40,877)	(37,888)
Net cash used in operating activities	(63,953)	(55,276)
Cash flows from investing activities:		
Purchases of property and equipment	(3,594)	(3,684)
Decrease in restricted cash		6,151
Purchases of marketable securities	(287,493)	(399,943)
Sales and maturities of marketable securities	261,346	366,290
Investment in joint venture (Regulus Therapeutics Inc.)		(10,000)
Net cash used in investing activities	(29,741)	(41,186)
Cash flows from financing activities:		
Proceeds from issuance of common stock	2,143	1,720
Proceeds from issuance of shares to Novartis	993	1,154
Net cash provided by financing activities	3,136	2,874
Effect of exchange rate on cash	(29)	(117)
Net decrease in cash and cash equivalents	(90,587)	(93,705)
Cash and cash equivalents, beginning of period	137,468	191,792
Cash and cash equivalents, end of period	\$ 46,881	\$ 98,087

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

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

1. SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES***Basis of Presentation and Principles of Consolidation***

The accompanying condensed consolidated financial statements of Alnylam Pharmaceuticals, Inc. (the Company or Alnylam) are unaudited and have been prepared in accordance with accounting principles generally accepted in the United States of America (GAAP) applicable to interim periods and, in the opinion of management, include all normal and recurring adjustments that are necessary to present fairly the results of operations for the reported periods. The Company's condensed consolidated financial statements have also been prepared on a basis substantially consistent with, and should be read in conjunction with, the Company's audited consolidated financial statements for the year ended December 31, 2009, 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 26, 2010. The year-end condensed balance sheet data was derived from audited financial statements, but does not include all disclosures required by GAAP. The results of the Company's operations for any interim period are not necessarily indicative of the results of the Company's operations for any other interim period or for a full fiscal year.

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

Reclassifications

Certain reclassifications have been made to prior years' condensed consolidated financial statements to conform to the 2010 presentation.

Use of Estimates

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

Net Loss Per Common Share

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

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

	Three and Nine Months Ended September 30,	
	2010	2009
Options to purchase common stock	7,915	6,792
Unvested restricted common stock		29
	7,915	6,821

Table of Contents**Fair Value Measurements**

The following tables present information about the Company's assets that are measured at fair value on a recurring basis as of September 30, 2010 and December 31, 2009, and indicate the fair value hierarchy of the valuation techniques the Company utilized to determine such fair value. In general, fair values determined by Level 1 inputs utilize quoted prices (unadjusted) in active markets for identical assets or liabilities. Fair values determined by Level 2 inputs utilize data points that are observable, such as quoted prices (adjusted), interest rates and yield curves. Fair values determined by Level 3 inputs utilize unobservable data points for the asset or liability, and include situations where there is little, if any, market activity for the asset or liability. Financial assets measured at fair value on a recurring basis are summarized as follows, in thousands:

Description	As of September 30, 2010	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	\$ 43,352	\$ 28,756	\$ 14,596	\$
Marketable securities (fixed income)				
Government obligations	156,263		156,263	
Corporate notes	138,321		138,321	
Commercial paper	25,973		25,973	
Municipal notes	1,800		1,800	
Marketable securities (equity holdings)	2,632		2,632	
Total	\$ 368,341	\$ 28,756	\$ 339,585	\$

Description	As of December 31, 2009	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
Cash equivalents	\$ 129,113	\$ 129,113	\$	\$
Marketable securities (fixed income)				
Government obligations	185,087		185,087	
Corporate notes	89,220		89,220	
Commercial paper	12,994		12,994	
Municipal notes	8,700		8,700	
Marketable securities (equity holdings)	1,847		1,847	
Total	\$ 426,961	\$ 129,113	\$ 297,848	\$

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.

Subsequent Events

The Company evaluated all events or transactions that occurred after September 30, 2010 up through the date these condensed consolidated financial statements were issued. During this period, the Company did not have any material

recognizable subsequent events. However, the Company did have the following unrecognizable subsequent events, which are more fully described in Notes 4 and 7:

As part of the June 2010 alliance, in October 2010, sanofi-aventis made a \$10.0 million equity investment in Regulus. See Note 4.

In November 2010, the Company, Medtronic Inc. (Medtronic) and CHDI Foundation, Inc. (CHDI) formed a collaboration to advance ALN-HTT, a novel drug-device combination for the treatment of Huntington s disease. See Note 7.

Table of Contents**Recent Accounting Pronouncements**

In April 2010, the Financial Accounting Standards Board (FASB) issued a new accounting standard, which provides guidance in applying the milestone method of revenue recognition to research or development arrangements. Under this guidance, management may recognize revenue contingent upon the achievement of a milestone in the period in which the milestone is achieved only if the milestone meets all the criteria within the guidance to be considered substantive. This standard is effective on a prospective basis for research and development milestones achieved in fiscal years beginning on or after June 15, 2010. The Company is currently evaluating the potential impact of this accounting standard on its condensed consolidated financial statements, however the Company does not believe it will have a significant impact.

In October 2009, the FASB issued a new accounting standard, which amends existing revenue recognition accounting pronouncements and provides accounting principles and application guidance on whether multiple deliverables exist, how the arrangement should be separated, and the consideration allocated. This standard eliminates the requirement to establish the fair value of undelivered products and services and instead provides for separate revenue recognition based upon management's estimate of the selling price for an undelivered item when there is no other means to determine the fair value of that undelivered item. Previously, accounting principles required that the fair value of the undelivered item be the price of the item either sold in a separate transaction between unrelated third parties or the price charged for each item when the item is sold separately by the vendor. Determining the fair value using these methods was difficult when the product was not individually sold because of its unique features. If the fair value of all of the elements in the arrangement was not determinable, then revenue was deferred until all of the items were delivered or fair value was determined. This new approach is effective prospectively for revenue arrangements entered into or materially modified in fiscal years beginning on or after June 15, 2010. The Company is currently evaluating the potential impact of this accounting standard on its condensed consolidated financial statements.

In June 2009, the FASB issued a new accounting standard, which amends previously issued accounting guidance for the consolidation of a variable interest entity (VIE) to require an enterprise to determine whether its variable interest or interests give it a controlling financial interest in a VIE. This amended consolidation guidance for VIEs also replaces the existing quantitative approach for identifying which enterprise should consolidate a VIE, which was based on which enterprise was exposed to a majority of the risks and rewards, with a qualitative approach, based on which enterprise has both (1) the power to direct the economically significant activities of the entity and (2) the obligation to absorb losses of the entity that could potentially be significant to the VIE or the right to receive benefits from the entity that could potentially be significant to the VIE. This new accounting standard has broad implications and may affect how the Company accounts for the consolidation of common structures, such as joint ventures, equity method investments, collaboration and other agreements, and purchase arrangements. Under this revised consolidation guidance, more entities may meet the definition of a VIE, and the determination about which entity should consolidate a VIE is required to be evaluated continuously. The Company adopted this standard effective January 1, 2010 and has determined that the adoption did not have an impact on its condensed consolidated financial statements.

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		Nine Months Ended	
	September 30,		September 30,	
	2010	2009	2010	2009
Roche	\$ 13,995	\$ 13,844	\$ 41,983	\$ 41,639
Takeda	5,556	5,438	16,479	16,274
Novartis	3,984	2,182	8,957	7,104
Government contract	1,008	1,410	4,095	5,144
Cubist	591	714	1,772	2,081
Other	2,534	661	5,563	1,665

Total net revenues from research collaborators	\$ 27,668	\$ 24,249	\$ 78,849	\$ 73,907
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In July 2007, the Company and, for limited purposes, Alnylam Europe, entered into a license and collaboration agreement (the LCA) with F. Hoffmann-La Roche Ltd (Roche Basel) and Hoffmann-La Roche Inc. (together with Roche Basel, Roche). Under the LCA, which became effective in August 2007, the Company granted Roche a non-exclusive license to the Company s intellectual property to develop and commercialize therapeutic products that function through RNA interference (RNAi), subject to the Company s existing contractual obligations to third parties. The license is initially limited to the therapeutic areas of oncology, respiratory diseases, metabolic diseases and certain liver diseases, and may be expanded to include up to 18 additional therapeutic areas, comprising substantially all other fields of human disease, as identified and agreed upon by the parties, upon payment to the Company by Roche of an additional \$50.0 million for each additional therapeutic area, if any.

In consideration for the rights granted to Roche under the LCA, Roche paid the Company \$273.5 million in upfront cash payments. In addition, in exchange for the Company s contributions under the LCA, for each RNAi therapeutic product developed by Roche, its affiliates or sublicensees under the LCA, the Company is entitled to receive milestone payments upon achievement of specified development and sales events, totaling up to an aggregate of \$100.0 million per therapeutic target, together with royalty payments based on worldwide annual net sales, if any.

Under the LCA, the Company and Roche also agreed to collaborate on the discovery of RNAi therapeutic products directed to one or more disease targets (Discovery Collaboration), subject to the Company s existing contractual obligations to third parties. In October 2009, the Company and Roche advanced their alliance to initiate this therapeutic collaboration stage, which is focused on advancing specific disease targets to develop RNAi therapeutics. Under this Discovery Collaboration, the Company and Roche are collaborating on the discovery and development of specific RNAi therapeutic products and each party is contributing key delivery technologies in this effort. The Company and Roche are co-developing and intend to co-commercialize RNAi therapeutic products in the U.S. market and the Company is eligible to receive additional milestone and royalty payments for products developed in the rest of the world, if any. After a pre-specified period of collaborative activities, each party will have the option to opt-out of the day-to-day development activities in exchange for reduced milestones and royalty payments in the future. The Discovery Collaboration is governed by the joint steering committee that is comprised of an equal number of representatives from each party.

In July 2007, the Company executed a common stock purchase agreement (the Common Stock Purchase Agreement) with Roche Finance Ltd, an affiliate of Roche (Roche Finance). Under the terms of the Common Stock Purchase Agreement, on August 9, 2007, Roche Finance purchased 1,975,000 shares of the Company s common stock at \$21.50 per share, for an aggregate purchase price of \$42.5 million. The Company recorded this issuance using the closing price of the Company s common stock on August 9, 2007, the date the shares were issued to Roche. Based on the closing price of \$25.98, the fair value of the shares issued was \$51.3 million, which was \$8.8 million in excess of the proceeds received from Roche for the issuance of the Company s common stock. As a result, the Company allocated \$8.8 million of the upfront payment from the LCA to the common stock issuance.

Under the terms of the Common Stock Purchase Agreement, in the event the Company proposes to sell or issue any of its equity securities, subject to specified exceptions, it agreed to grant to Roche Finance the right to acquire, at fair value, additional securities, such that Roche Finance would be able to maintain its ownership percentage in the Company.

In connection with the execution of the LCA and the Common Stock Purchase Agreement, the Company also executed a share purchase agreement (the Alnylam Europe Purchase Agreement) with Alnylam Europe and Roche Beteiligungs GmbH, an affiliate of Roche (Roche Germany). Under the terms of the Alnylam Europe Purchase Agreement, which became effective in August 2007, the Company created a new, wholly-owned German limited liability company (Roche Kulmbach) into which substantially all of the non-intellectual property assets of Alnylam Europe were transferred, and Roche Germany purchased from the Company all of the issued and outstanding shares of Roche Kulmbach for an aggregate purchase price of \$15.0 million. The Alnylam Europe Purchase Agreement also included transition services that were performed by Roche Kulmbach employees at various levels through August 2008. The Company reimbursed Roche for these services at an agreed-upon rate.

In summary, the Company received upfront payments totaling \$331.0 million under the Roche alliance, which included an upfront payment under the LCA of \$273.5 million, \$42.5 million under the Common Stock Purchase Agreement and \$15.0 million for the Roche Kulmbach shares under the Alnylam Europe Purchase Agreement. The Company initially recorded \$278.2 million of these proceeds as deferred revenue in connection with the Roche alliance. The Company allocated \$51.3 million and \$1.5 million to the common stock issuance and the net book value of Alnylam Europe, respectively.

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When evaluating multiple element arrangements, the Company considers whether the components of the arrangement represent separate units of accounting. The accounting guidance specifically requires that the delivered components must have value to the customer on a standalone basis and that there is objective and reliable evidence of the fair value of the undelivered components. Application of this standard requires subjective determinations and requires management to make judgments about the value of each individual element and whether it is separable from the other aspects of the contractual relationship. The Company has determined that the deliverables under the Roche alliance include the license, the Alnylam Europe assets and employees, the steering committees (joint steering committee and future technology committee) and the services that the Company is obligated to perform under the Discovery Collaboration. The Company has determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the license and assets of Alnylam Europe are not separable from the undelivered services (i.e., the steering committees and Discovery Collaboration) and, accordingly the license and the services are being treated as a single unit of accounting. When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition pattern on the final deliverable. Under the Roche alliance, the steering committee services and the Discovery Collaboration services are the final deliverables and all such services will end, contractually, five years from the effective date of the LCA.

The Company is recognizing the Roche-related revenue on a straight-line basis over five years because the Company cannot reasonably estimate the total level of effort required to complete its service obligations under the LCA in order to utilize a proportional performance model. As future substantive milestones are achieved, 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, will be recognized as revenue upon achievement of such milestone. The remaining portion of the milestone will be recognized over the remaining performance period on a straight-line basis.

Takeda Alliance

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

In consideration for the rights granted to Takeda under the Takeda Collaboration Agreement, Takeda agreed to pay the Company \$150.0 million in upfront and near-term technology transfer payments. In addition, the Company has the option, exercisable until the start of Phase III development, to opt-in under a 50-50 profit sharing agreement to the development and commercialization in the United States of up to four Takeda licensed products, and would be entitled to opt-in rights for two additional products for each additional field expansion, if any, elected by Takeda under the Takeda Collaboration Agreement. In June 2008, Takeda paid the Company an upfront payment of \$100.0 million and agreed to pay an additional \$50.0 million to the Company upon achievement of specified technology transfer milestones (the Technology Transfer Milestones). Of this \$50.0 million, \$20.0 million was paid in October 2008, \$20.0 million was paid in March 2010, and \$10.0 million is due upon achievement of the last specified technology transfer activities, but no later than the second quarter of 2011. If Takeda elects to expand its license to additional therapeutic areas, Takeda will be required to pay the Company \$50.0 million for each of up to approximately 20 total additional fields selected, if any, comprising substantially all other fields of human disease, as identified and agreed upon by the parties. In addition, for each RNAi therapeutic product developed by Takeda, its affiliates and sublicensees, the Company is entitled to receive specified development and commercialization milestones, totaling up to \$171.0 million per product, together with royalty payments based on worldwide annual net sales, if any.

Pursuant to the Takeda Collaboration Agreement, the Company and Takeda are also collaborating on the research of RNAi therapeutics directed to one or two disease targets agreed to by the parties (the Research Collaboration),

subject to the Company's existing contractual obligations with third parties. Takeda also has the option, subject to certain conditions, to collaborate with the Company on the research and development of RNAi drug delivery technology for targets agreed to by the parties. In addition, Takeda has a right of first negotiation for the development and commercialization of the Company's RNAi therapeutic products in the Asian territory, excluding the Company's ALN-RSV program. In addition to the 50-50 profit sharing option, the Company has a similar right of first negotiation to participate with Takeda in the development and commercialization in the United States of licensed products. The collaboration between the Company and Takeda is governed by a joint technology transfer committee (the JTTC), a joint research

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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.

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

The Company is recognizing the upfront payment of \$100.0 million, the first and second Technology Transfer Milestones of \$40.0 million, and the remaining Technology Transfer Milestone of \$10.0 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 in order to utilize a proportional performance model, primarily because the effort required under the Research Collaboration is largely unknown. As future substantive milestones are achieved, 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, will be recognized as revenue upon achievement of such milestone. The remaining portion of the milestone will be recognized over the remaining performance period on a straight-line basis.

Discovery and Development Alliances***Isis Collaboration and License Agreement***

In April 2009, the Company and Isis Pharmaceuticals, Inc. (Isis) amended and restated their existing strategic collaboration and license agreement (as amended and restated, the Amended and Restated Isis Agreement), originally entered into in March 2004, to extend the broad cross-licensing arrangement regarding double-stranded RNAi that was established in 2004, pursuant to which Isis granted the Company licenses to its current and future patents and patent applications relating to chemistry and to RNA-targeting mechanisms for the research, development and commercialization of double-stranded RNA (dsRNA) products. The Company has the right to use Isis technologies in its development programs or in collaborations and Isis agreed not to grant licenses under these patents to any other organization for the discovery, development or commercialization of dsRNA products designed to work through an RNAi mechanism, except in the context of a collaboration in which Isis plays an active role. The Company granted Isis non-exclusive licenses to its current and future patents and patent applications relating to RNA-targeting mechanisms and to chemistry for research use. The Company also granted Isis the non-exclusive right to develop and commercialize dsRNA products developed using RNAi technology against a limited number of targets. In addition, the Company granted Isis non-exclusive rights to research, develop and commercialize single-stranded RNA products.

Under the terms of the Isis agreement, the Company paid Isis an upfront license fee of \$5.0 million. The Company also agreed to pay Isis milestone payments, totaling up to approximately \$3.4 million, upon the occurrence of specified development and regulatory events, and royalties on sales, if any, for each product that the Company or a collaborator develops using Isis intellectual property. In addition, the Company agreed to pay to Isis a percentage of specified fees from strategic collaborations the Company may enter into that include access to Isis intellectual property.

Isis agreed to pay the Company, per therapeutic target, a license fee of \$0.5 million, and milestone payments totaling approximately \$3.4 million, payable upon the occurrence of specified development and regulatory events, and royalties on sales, if any, for each product developed by Isis or a collaborator that utilizes the Company's intellectual property. Isis has the right to elect up to ten non-exclusive target licenses under the agreement and has the right to purchase one additional non-exclusive target per year during the term of the collaboration.

As part of the Amended and Restated Isis Agreement, the Company and Isis established a collaborative effort focused on the development of single-stranded RNAi (ssRNAi) technology. Under the Amended and Restated Isis Agreement, the Company obtained from Isis a co-exclusive, worldwide license to Isis current and future patents and

patent applications relating to chemistry and RNA-targeting mechanisms to research, develop and commercialize ssRNAi products. Each of the Company and Isis has the opportunity to discover and develop drugs employing the ssRNAi technology. Under the terms of the Amended and Restated Isis Agreement, the Company will potentially pay Isis up to an aggregate of \$31.0 million in license fees, payable in four tranches, that include \$11.0 million paid on signing, \$10.0 million payable if and when the Company determines to move forward with the

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collaborative effort, or if and when *in vivo* efficacy in rodents is demonstrated, if sooner, \$5.0 million upon achievement of *in vivo* efficacy in non-human primates, and \$5.0 million upon initiation of the first clinical trial with an ssRNAi drug, subject to the Company's right to unilaterally terminate the ssRNAi research program. The Company is also obligated to fund certain research activities at a minimum of \$3.0 million each year for three years with research and development activities conducted by both the Company and Isis. If the Company develops and commercializes drugs utilizing ssRNAi technology on its own or with a partner, the Company would be required to make milestone payments to Isis, totaling up to \$18.5 million per product, as well as royalties. Also, Isis initially is eligible to receive up to 50% of any sublicense payments due to the Company from a third party based on the Company's partnering of ssRNAi products, which amount will decline over time as the Company's investment in the technology and drugs increases. In turn, the Company is eligible to receive up to five percent of any sublicense payments due to Isis from a third party based on Isis' partnering of ssRNAi products.

The Company's unilateral right to terminate the ssRNAi research program has been mutually extended by the parties from September 30, 2010 into the fourth quarter of 2010. During this extension, the Company's obligation to provide research funding has been suspended. In the event that the Company terminates the research program, any licenses to ssRNAi products granted by Isis to the Company under the Amended and Restated Isis Agreement, and any obligation thereunder by the Company to provide additional research funding or pay additional license fees, milestone payments, royalties or sublicense payments to Isis for such ssRNAi products, would also terminate.

The Company's accounting policy is to classify license fees, milestone payments and sublicense payments made to Isis as research and development expenses.

Novartis Broad Alliance

In the second half of 2005, the Company entered into a series of transactions with Novartis Pharma AG and its affiliate, Novartis Institutes for BioMedical Research, Inc. (collectively, *Novartis*). In September 2005, the Company and Novartis executed a stock purchase agreement (the *Stock Purchase Agreement*) and an investor rights agreement (the *Investor Rights Agreement*). In October 2005, in connection with the closing of the transactions contemplated by the Stock Purchase Agreement, the Investor Rights Agreement became effective and the Company and Novartis executed a research collaboration and license agreement (the *Collaboration and License Agreement*). The Collaboration and License Agreement had an initial term of three years, with an option for two additional one-year extensions at the election of Novartis. In July 2009, Novartis elected to further extend the term for the fifth and final planned year, through October 2010. In October 2010, the research program under the Collaboration and License Agreement was substantially completed in accordance with the terms of the Collaboration and License Agreement, subject to certain surviving rights and obligations of the parties.

Under the terms of the Stock Purchase Agreement, in October 2005, Novartis purchased 5,267,865 shares of the Company's common stock at a purchase price of \$11.11 per share for an aggregate purchase price of \$58.5 million, which, after such issuance, represented 19.9% of the Company's outstanding common stock as of the date of issuance. In addition, under the Investor Rights Agreement, the Company granted Novartis rights to acquire additional equity securities in the event that the Company proposes to sell or issue any equity securities, subject to specified exceptions, as described in the Investor Rights Agreement, such that Novartis would be able to maintain its then-current ownership percentage in the Company's outstanding common stock. Pursuant to terms of the Investor Rights Agreement, in May 2008, Novartis purchased 213,888 shares of the Company's common stock at a purchase price of \$25.29 per share, resulting in a payment to the Company of \$5.4 million. In May 2009, Novartis purchased 65,922 shares of the Company's common stock at a purchase price of \$17.50 per share, resulting in an aggregate payment to the Company of \$1.2 million. In April 2010, Novartis purchased 55,223 shares of the Company's common stock at a purchase price of \$17.99 per share, resulting in an aggregate payment to the Company of \$1.0 million. These purchases have allowed Novartis to maintain its ownership position of approximately 13.4% of the Company's outstanding common stock. The exercises of this right did not result in any changes to existing rights or any additional rights to Novartis. Further, during the term described in the Investor Rights Agreement, Novartis is permitted to own no more than 19.9% of the Company's outstanding shares.

In consideration for the rights granted to Novartis under the Collaboration and License Agreement, Novartis made upfront payments totaling \$10.0 million to the Company in October 2005, partly to reimburse prior costs incurred by

the Company to develop *in vivo* RNAi technology, together with research funding and development milestone payments.

In September 2010, Novartis exercised its right under the Collaboration and License Agreement to select 31 designated gene targets, for which Novartis has exclusive rights to discover, develop and commercialize RNAi therapeutic products using the Company's intellectual property and technology. Under the terms of the Collaboration and License Agreement, for any RNAi therapeutic products Novartis develops against these targets, the Company is entitled to receive milestone payments upon achievement of certain specified development and annual net sales events, up to an aggregate of \$75.0 million per therapeutic product, as well as royalties on annual net sales of any such product. In September 2010, Novartis also notified the Company that it had declined to

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exercise its non-exclusive option to integrate into its operations the Company's fundamental and chemistry intellectual property under the terms of the Collaboration and License Agreement. If Novartis had elected to exercise the integration option, Novartis would have been required to make additional payments to the Company totaling \$100.0 million.

The Company initially deferred the non-refundable \$10.0 million upfront payment and the \$6.4 million premium received that represented the difference between the purchase price and the closing price of the common stock of the Company on the date of the stock purchase from Novartis. These payments, in addition to research funding and certain milestone payments, the receipt of which is considered probable, together total \$64.6 million, and are being amortized into revenue using the proportional performance method over the estimated duration of the Collaboration and License Agreement, or ten years. Under this model, the Company estimates the level of effort to be expended over the term of the agreement and recognizes revenue based on the lesser of the amount calculated based on proportional performance of total expected revenue or the amount of non-refundable payments earned.

As future substantive milestones are achieved, and to the extent they are within the period of performance, milestone payments will be recognized as revenue on a proportional performance basis over the contract's entire performance period, starting with the contract's commencement. A portion of the milestone payment equal to the percentage of total performance completed when the milestone is achieved, multiplied by the milestone payment, will be recognized as revenue upon achievement of the milestone. The remaining portion of the milestone will be recognized over the remaining performance period under the proportional performance method.

The Company believes the estimated period of performance under the Collaboration and License Agreement is ten years, which includes the three-year initial term of the agreement, two one-year extensions elected by Novartis and limited support as part of a technology transfer until 2015, the fifth anniversary of the termination of the Collaboration and License Agreement. The Company continues to use an expected term of ten years in its proportional performance model. The Company reevaluates the expected term when new information is known that could affect the Company's estimate. In the event the Company's period of performance is different than estimated, revenue recognition will be adjusted on a prospective basis.

Product Alliances*Kyowa Hakko Kirin Alliance*

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

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

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

The Company has determined that the deliverables under the Kyowa Hakko Kirin Agreement include the license, the joint steering committee, the manufacturing services and any Additional Compounds. The Company has determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the individual deliverables are not separable and, accordingly, must be accounted for as a single unit of accounting. When multiple deliverables are accounted for as a single unit

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of accounting, the Company bases its revenue recognition pattern on the final deliverable. The Company is currently unable to reasonably estimate its period of performance under the Kyowa Hakko Kirin Agreement, as it is unable to estimate the timeline of its deliverables related to the fixed-price option granted to Kyowa Hakko Kirin for any Additional Compounds. The Company is deferring all revenue under the Kyowa Hakko Kirin Agreement until it is able to reasonably estimate its period of performance. The Company will continue to reassess whether it can reasonably estimate the period of performance to fulfill its obligations under the Kyowa Hakko Kirin Agreement.

Cubist Alliance

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

Under the terms of the *Cubist Agreement*, the Company and Cubist share responsibility for developing Licensed Products in North America and each bears one-half of the related development costs, subject to the terms of the *Amendment*. The Company's collaboration with Cubist for the development of Licensed Products in North America is governed by a joint steering committee comprised of an equal number of representatives from each party. Cubist will have the sole right to commercialize Licensed Products in North America with costs associated with such activities and any resulting profits or losses to be split equally between the Company and Cubist. Throughout the rest of the world (the *Royalty Territory*), excluding Asia, where the Company has previously partnered its ALN-RSV program with Kyowa Hakko Kirin, Cubist has an exclusive, royalty-bearing license to develop and commercialize Licensed Products.

In consideration for the rights granted to Cubist under the *Cubist Agreement*, in January 2009, Cubist made a \$20.0 million upfront cash payment to the Company. Cubist also has an obligation under the *Cubist Agreement* to pay the Company milestone payments, totaling up to an aggregate of \$82.5 million, upon the achievement of specified development and sales events in the *Royalty Territory*. In addition, if Licensed Products are successfully developed, Cubist will be required to pay to the Company royalties on net sales of Licensed Products in the *Royalty Territory*, if any, subject to offsets under certain circumstances. Upon achievement of certain development milestones, the Company will have the right to convert the North American co-development and profit sharing arrangement into a royalty-bearing license and, in addition to royalties on net sales in North America, will be entitled to receive additional milestone payments totaling up to an aggregate of \$130.0 million upon achievement of specified development and sales events in North America, subject to the timing of the conversion by the Company and the regulatory status of Licensed Products at the time of conversion. If the Company makes the conversion to a royalty-bearing license with respect to North America, then North America becomes part of the *Royalty Territory*.

During the term of the *Cubist Agreement*, neither party nor its affiliates may develop, manufacture or commercialize anywhere in the world, outside of Asia, a therapeutic or prophylactic product that specifically targets RSV, except for Licensed Products developed, manufactured or commercialized pursuant to the *Cubist Agreement*.

The Company has determined that the deliverables under the *Cubist Agreement* include the licenses, technology transfer related to the ALN-RSV program, the joint steering committee and the development and manufacturing services that the Company is obligated to perform during the development period. The Company also has determined that, pursuant to the accounting guidance governing revenue recognition on multiple element arrangements, the licenses and undelivered services are not separable and, accordingly, the licenses and services are being treated as a

single unit of accounting. When multiple deliverables are accounted for as a single unit of accounting, the Company bases its revenue recognition pattern on the final deliverable. Under the Cubist Agreement, the last element to be delivered is the development and manufacturing services, which have an expected life of approximately eight years.

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The Company is recognizing the upfront payment of \$20.0 million on a straight-line basis over approximately eight years because the Company is unable to reasonably estimate the level of effort to fulfill its performance obligations in order to utilize a proportional performance model. As future substantive milestones are achieved, 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, will be recognized as revenue upon achievement of such milestone. The remaining portion of the milestone will be recognized over the remaining performance period on a straight-line basis.

Under the terms of the Cubist Agreement, the Company and Cubist share responsibility for developing Licensed Products in North America and each bears one-half of the related development costs, provided that under the terms of the Amendment, the Company is funding the advancement of ALN-RSV01 for adult lung transplant patients and Cubist retains an opt-in right. For revenue generating arrangements that involve cost sharing between the parties, the Company presents the results of activities for which it acts as the principal on a gross basis and reports any payments received from (made to) other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, analogy to authoritative accounting literature or a reasonable, rational and consistently applied accounting policy election. As the Company is not considered the principal under the Cubist Agreement, the Company records any amounts due from Cubist as a reduction of research and development expense. For the three and nine months ended September 30, 2010, the Company and Cubist incurred costs of \$0.6 million and \$1.6 million, respectively, under the Cubist Agreement, of which \$0.5 million and \$1.4 million, respectively, was incurred by the Company. For the three and nine months ended September 30, 2009, the Company and Cubist incurred costs of \$2.9 million and \$9.9 million, respectively, of which \$2.8 million and \$9.6 million, respectively, was incurred by the Company. During the three and nine months ended September 30, 2010, amounts due from Cubist of \$0.2 million and \$0.6 million, respectively, were recorded by the Company as a reduction to research and development expense. During the three and nine months ended September 30, 2009, amounts due from Cubist of \$1.3 million and \$4.6 million, respectively, were recorded by the Company as a reduction to research and development expense. As such, the Company recorded net research and development expenses in its condensed consolidated statements of operations of \$0.3 million and \$0.8 million for the three and nine months ended September 30, 2010, respectively, and \$1.5 million and \$5.0 million for the three and nine months ended September 30, 2009, respectively.

In connection with the Cubist Agreement, during 2009, the Company paid \$1.0 million of license fees to the Company's licensors, primarily Isis, in accordance with the applicable license agreements with those parties. These fees were charged to research and development expense.

Government Funding*NIH Contract*

In September 2006, the National Institute of Allergy and Infectious Diseases (NIAID), a component of the National Institutes of Health (NIH), awarded the Company a contract for up to \$23.0 million over four years to advance the development of a broad spectrum RNAi anti-viral therapeutic for hemorrhagic fever virus, including the Ebola virus. As a result of the continued progress of this program, the NIAID has appropriated the entire \$23.0 million over the four-year term of the contract, which was originally expected to be completed in September 2010. The Company and the NIAID have agreed to a no-cost extension of the contract through December 2010 during which time the funds remaining under the contract will be available to the Company. The Company recognizes revenue under government cost reimbursement contracts as it performs the underlying research and development activities. At September 30, 2010, there was \$0.2 million of remaining funds available under the NIAID contract.

3. INCOME TAXES

During the three and nine months ended September 30, 2010, the Company recorded a provision for income taxes of \$0.3 million and \$0.1 million, respectively. The provision for income taxes in 2010 was due primarily to a tax reserve recorded for uncertain tax positions of \$0.3 million. During the three and nine months ended September 30, 2009, the Company recorded a benefit from income taxes of \$0.6 million and a provision for income taxes of \$1.0 million, respectively. The provision for income taxes in 2009 was due primarily to taxable income in 2009 as a result of the Company's alliances with Roche and Takeda. The Company expects to generate U.S. taxable losses during 2010. The Company's 2010 U.S. taxable losses are expected to be carried back to 2008 and 2009 to offset

taxable income generated to the extent of the federal alternative minimum taxable income in those years.

At December 31, 2009, the Company recorded net deferred tax assets to the extent it is more likely than not that the assets will be utilized. These deferred tax assets were related to the recognition of Roche and Takeda revenue for tax purposes. The Company expects to generate net operating losses in 2010 that will be carried back to 2008 and 2009 to offset taxable income. The remaining deferred tax assets are subject to a valuation allowance as it is more likely than not that those assets will not be realized. If the Company does not generate sufficient tax losses, it could affect the realizability of its deferred tax assets.

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At December 31, 2009, the state net operating loss carryforward was \$8.6 million. This attribute is available to reduce the Company's future California state tax liability and expires at various dates through 2018. Ownership changes, as defined in the Internal Revenue Code, including those resulting from the issuance of common stock in connection with the Company's public offerings, may limit the amount of net operating loss that can be utilized to offset future taxable income or tax liability. The Company has determined that there is no limitation on the utilization of net operating loss carryforwards in accordance with Section 382 of the Internal Revenue Code. The Company is currently under audit by the Internal Revenue Service for the 2008 tax year. The Company believes that it has provided sufficiently for all significant audit exposures.

4. REGULUS

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

In consideration for the Company's and Isis' initial interests in Regulus, each party granted Regulus exclusive licenses to its intellectual property for certain microRNA therapeutic applications as well as certain patents in the microRNA field. In addition, the Company made an initial cash contribution to Regulus of \$10.0 million, resulting in the Company and Isis making approximately equal aggregate initial capital contributions to Regulus. In March 2009, the Company and Isis each purchased \$10.0 million of Series A preferred stock of Regulus under a founder's investor rights agreement (the "Investor Rights Agreement"). As of September 30, 2010, the Company and Isis owned approximately 49% and 51%, respectively, of Regulus and there were no other third-party investors in Regulus. The Company has concluded that Regulus is a related party. Regulus continues to operate as an independent company with a separate board of directors, scientific advisory board and management team, some of whom have options to purchase common stock of Regulus. Members of the board of directors of Regulus who are employees of the Company or Isis are not eligible to receive options to purchase Regulus common stock.

In April 2008, Regulus entered into a worldwide strategic alliance with GlaxoSmithKline ("GSK") to discover, develop and commercialize up to four novel microRNA-targeted therapeutics to treat inflammatory diseases such as rheumatoid arthritis and inflammatory bowel disease. In connection with this alliance, Regulus received \$20.0 million in upfront payments from GSK, including a \$15.0 million option fee and a loan of \$5.0 million (guaranteed by Isis and the Company) that will convert into Regulus common stock under certain specified circumstances. Regulus could be eligible to receive development, regulatory and sales milestone payments for each of the microRNA-targeted therapeutics discovered and developed as part of the alliance. Regulus would also receive royalty payments on worldwide sales of products resulting from the alliance, if any.

In February 2010, Regulus and GSK established a new collaboration to develop and commercialize microRNA therapeutics targeting miR-122 in all fields, with the treatment of hepatitis C virus infection as the lead indication. Under the terms of this new collaboration, Regulus received \$8.0 million in upfront payments from GSK, including a \$3.0 million license fee and a loan of \$5.0 million (guaranteed by Isis and the Company) that will convert into Regulus common stock under certain specified circumstances. Consistent with the original GSK alliance, Regulus could be eligible to receive development, regulatory and sales milestone payments, as well as royalty payments on worldwide sales of products resulting from the alliance, if any, as Regulus and GSK advance microRNA therapeutics targeting miR-122.

In June 2010, Regulus entered into a global, strategic alliance with sanofi-aventis to discover, develop and commercialize microRNA therapeutics on up to four microRNA targets. Under the terms of this new alliance, Regulus received \$25.0 million in upfront fees and is entitled to annual research support for three years with the option to extend research support for two additional years. As part of this alliance, in October 2010, sanofi-aventis made a \$10.0 million equity investment in Regulus, resulting in sanofi-aventis owning approximately 9% of Regulus. Following this investment, the Company and Isis own approximately 45% and 46%, respectively, of Regulus.

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In addition, Regulus is eligible to receive royalties on microRNA therapeutic products commercialized by sanofi-aventis, if any. Sanofi-aventis will support 100% of the costs of clinical development and commercialization of each program. The alliance will initially focus on the therapeutic area of fibrosis. Regulus and sanofi-aventis will collaborate on up to four microRNA targets, including Regulus lead fibrosis program targeting microRNA-21. Sanofi-aventis also received an option for a broader technology alliance with Regulus that provides Regulus certain rights to participate in development and commercialization of resulting products. If exercised, this option is worth up to an additional \$50.0 million to Regulus. The Company and Isis are each eligible to receive 7.5% of all potential milestone payments in addition to royalties on product sales, if any. In addition, for the nine months ended September 30, 2010, the Company has recognized \$1.9 million in related-party revenues in its condensed consolidated statements of operations, representing 7.5% of the \$25.0 million upfront payment from sanofi-aventis to Regulus.

The Company has reviewed the consolidation guidance that defines a VIE and concluded that Regulus currently qualifies as a VIE. The Company does not consolidate Regulus as the Company lacks the power to direct the activities that could significantly impact the economic success of this entity. At September 30, 2010, the total carrying value of the Company's investment in joint venture (Regulus Therapeutics Inc.) in its condensed consolidated balance sheets is \$20,000 under the equity method. The Company's maximum exposure to loss related to this VIE is limited to the carrying value of the Company's investment, as well the portion of Regulus' debt, including accrued interest, guaranteed by the Company which was \$5.3 million at September 30, 2010. Under new consolidation guidance effective January 1, 2010, Isis is no longer consolidating Regulus' financial statements.

The Company accounts for its investment in Regulus using the equity method of accounting. Through December 31, 2008, the Company was recognizing 100% of the first \$10.0 million of losses of Regulus as equity in loss of joint venture (Regulus Therapeutics Inc.) in its condensed consolidated statements of operations because the Company was responsible for funding those losses through its initial \$10.0 million cash contribution. Beginning in January 2009, in connection with the conversion of Regulus to a C corporation, through September 30, 2010, the Company has recognized approximately 49% of the losses of Regulus. The carrying value of the Company's investment in joint venture (Regulus Therapeutics Inc.), immediately prior to the conversion to a C corporation exceeded 49% of the net assets of Regulus by approximately \$0.8 million. Upon conversion, this amount was allocated to the intellectual property of Regulus and, because the intellectual property was determined to be in-process research and development, the \$0.8 million was recorded as a charge to expense. This charge is included in equity in loss of joint venture (Regulus Therapeutics Inc.) in the Company's condensed consolidated statements of operations for the nine months ended September 30, 2009. Under the equity method, the reimbursement of expenses to the Company is recorded as a reduction to research and development expenses. Summary results of Regulus' operations for the three and nine months ended September 30, 2010 and 2009 and balance sheets as of September 30, 2010 and December 31, 2009 are presented below, in thousands (unaudited):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2010	2009	2010	2009
Statement of Operations Data:				
Net revenues	\$ 2,309	\$ 625	\$ 3,804	\$ 2,388
Operating expenses (1)	4,743	2,935	17,182	8,302
Loss from operations	(2,434)	(2,310)	(13,378)	(5,914)
Other (expense) income	(48)	11	(132)	23
Net loss	\$ (2,482)	\$ (2,299)	\$ (13,510)	\$ (5,891)
(1) Non-cash stock-based compensation expenses included in operating expenses	\$ 128	\$ 207	\$ 429	\$ (14)

	September 30, 2010	December 31, 2009
Balance Sheet Data:		
Cash, cash equivalents and marketable securities	\$ 50,020	\$ 30,708
Working capital	37,108	25,115
Total assets	53,951	32,930
Notes payable	11,269	6,291
Total stockholders (deficit) equity	(120)	12,939

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In May 2010, the Company entered into an amendment to its lease with ARE-MA Region No. 28 LLC (the Landlord), dated as of September 26, 2003, as amended (the Amended Lease), pursuant to which the Company is renting approximately 34,000 square feet of additional laboratory and office space located at 300 Third Street, Cambridge, Massachusetts (the Premises), effective as of October 1, 2010. The Company leases a total of approximately 129,000 square feet of office and laboratory space at the Premises under the Amended Lease. The term of the Amended Lease expires in September 2016. The Company has the option to extend the Amended Lease for two successive five-year extensions. As a result, the Company's operating lease obligations through 2016 increased by an aggregate of \$8.9 million as a result of the Amended Lease, partially offset by future sublease payments to the Company of \$1.7 million, resulting in a net increase of \$7.2 million. The Company has separately agreed to sublease the first floor of the Premises through the end of 2011.

Litigation

In June 2009, the Company joined with Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften E.V. and Max-Planck-Innovation GmbH (collectively, Max Planck) in taking legal action against the Whitehead Institute for Biomedical Research (Whitehead), the Massachusetts Institute of Technology (MIT) and the Board of Trustees of the University of Massachusetts (UMass). The complaint, initially filed in the Suffolk County Superior Court in Boston, Massachusetts and subsequently removed to the U.S. District Court for the District of Massachusetts, alleges, among other things, that the defendants have improperly prosecuted the so-called Tuschl I patent applications and wrongfully incorporated inventions covered by the so-called Tuschl II patent applications into the Tuschl I patent applications, thereby potentially damaging the value of inventions reflected in the Tuschl I and Tuschl II patent applications. In the field of RNAi therapeutics, the Company is the exclusive licensee of the Tuschl I patent applications from Max Planck, MIT and Whitehead, and of the Tuschl II patent applications from Max Planck.

The complaint seeks, among other things, a declaratory judgment regarding the prosecution of the Tuschl I patent family and unspecified monetary damages. In August 2009, Whitehead and UMass filed counterclaims against the Company and Max Planck, including for breach of contract. In January 2010, the Company and Max Planck filed an amended complaint expanding upon the allegations in the original complaint. The Company currently expects a jury trial to start in early 2011. In February 2010, the Company and Max Planck released MIT from any claims seeking monetary damages, and MIT has stipulated that it will be bound by any declaratory, injunctive, or equitable relief granted by the court.

In addition, in September 2009, the U.S. Patent and Trademark Office (USPTO) granted Max Planck's petition to revoke power of attorney in connection with the prosecution of the Tuschl I patent application. This action prevents the defendants from filing any papers with the USPTO in connection with further prosecution of the Tuschl I patent application without the agreement of Max Planck. Whitehead's petition to overturn this ruling was denied. Prosecution before the USPTO for both the Tuschl I and II pending patent applications was suspended pursuant to a standstill agreement. This agreement expired on September 15, 2010, and Max Planck, MIT, Whitehead and UMass agreed to file several continuation applications in the Tuschl I patent family to preserve their rights and maintain the status quo for these applications. Max Planck also filed a continuation application in the Tuschl II patent family.

Although the Company, along with Max Planck, are vigorously asserting their rights in this case, litigation is subject to inherent uncertainty and a court could ultimately rule against the Company and Max Planck. In addition, litigation is costly and may divert the attention of the Company's management and other resources that would otherwise be engaged in running the Company's business. The Company has not recorded an estimated liability associated with the legal proceedings described above due to the uncertainties related to both the likelihood and the amount of any potential loss.

6. RESTRUCTURING

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

implementing a reduction of the Company's overall workforce by approximately 25%.

During the three months ended September 30, 2010, the Company recorded \$2.2 million of restructuring related costs in operating expenses, including employee severance, benefits and related costs. These expenses are expected to be substantially paid by the end of the first half of 2011.

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The following table outlines the components of the Company's restructuring expenses recorded in operating expenses and in current liabilities for the three months ended September 30, 2010, in thousands:

	Expenses	Cash Paid	Amounts Accrued as of September 30, 2010
Employee severance, benefits and related costs	\$ 2,193	\$	\$ 2,193
Total	\$ 2,193	\$	\$ 2,193

7. SUBSEQUENT EVENT***CHDI Collaboration***

In November 2010, the Company, Medtronic and CHDI formed a collaboration to advance ALN-HTT, a novel drug-device combination for the treatment of Huntington's disease. ALN-HTT consists of an RNAi therapeutic targeting huntingtin, the gene responsible for Huntington's disease, that is being developed for delivery to the central nervous system using an implantable infusion system developed by Medtronic. CHDI is a not-for-profit virtual biotech company that is exclusively dedicated to rapidly discovering and developing therapies that slow the progression of Huntington's disease. The Company and Medtronic have been working collaboratively on advancing ALN-HTT for the treatment of Huntington's disease under a collaboration agreement, originally executed in 2005 and amended and restated in 2007 (the "Medtronic Agreement").

Under this new collaboration, CHDI has agreed to initially fund approximately 50% of the investigational new drug application-enabling activities, which represents over \$10.0 million in potential funding. The Medtronic Agreement will remain as a 50-50 partnership in the United States. With respect to the initial product development program focused on Huntington's disease, each of the Company and Medtronic is funding 50% of the development efforts for the United States. Medtronic will commercialize any resulting product consisting of the RNAi compound and delivery device. In the United States, the Company has the opportunity to invest in clinical development through product launch in return for a proportional share of the profits. In Europe, Medtronic is solely responsible for development and commercialization, and the Company is eligible to receive milestones and royalties on product sales, if any.

Table of Contents**ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS.**

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

Overview

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

We are applying our technological expertise to build a pipeline of RNAi therapeutics to address significant medical needs, many of which cannot effectively be addressed with small molecules or antibodies, the current major classes of drugs. We are working to develop RNAi therapeutics that are delivered directly to specific sites of disease, as well as RNAi therapeutics that are administered systemically through the bloodstream by intravenous, subcutaneous or intramuscular approaches.

Our lead RNAi therapeutic program, ALN-RSV01, is in Phase II clinical trials for the treatment of human respiratory syncytial virus, or RSV, infection, which is reported to be the leading cause of hospitalization in infants in the United States and also occurs in the elderly and in immune compromised adults. In February 2008, we reported positive results from our Phase II experimental RSV infection trial, referred to as the GEMINI study. In July 2009, we and Cubist Pharmaceuticals, Inc., or Cubist, reported results from a Phase IIa clinical trial assessing the safety and tolerability of aerosolized ALN-RSV01 versus placebo in adult lung transplant patients naturally infected with RSV. This clinical trial achieved its primary objective of demonstrating the safety and tolerability of ALN-RSV01. In particular, there were no drug-related serious adverse events or discontinuations, and there were no clinically significant differences in the overall adverse event profile between ALN-RSV01 and placebo. Importantly, there was no evidence of disease exacerbation related to ALN-RSV01 treatment. At the 90-day endpoint, all patients survived and the incidence of intubation, new respiratory infection or acute rejection was comparable across ALN-RSV01 and placebo groups. In addition, 90-day clinical data were collected. The trial was not powered to demonstrate clinical outcomes due to the small sample size and, accordingly, such data were therefore considered exploratory. Prospectively defined clinical secondary endpoints at 90 days included recovery of lung function (forced expiratory volume in the first second, or FEV₁) as measured by spirometry and clinical determination of new or progressive bronchiolitis obliterans syndrome, or BOS. Based on the data from this small trial, ALN-RSV01 treatment was associated with a statistically significant decrease in the total incidence of new or progressive BOS at 90 days compared to placebo (p=0.02) with 50% of placebo patients showing new or progressive BOS as compared with only 7.1% of ALN-RSV01-treated patients. Despite the small patient numbers, we believe that these data may be important

since the incidence of BOS following RSV infection in lung transplant patients can be a predictor of graft failure and overall survival. The incidence of BOS in lung transplant patients infected with RSV results in approximately 50% mortality within three to five years of onset.

In February 2010, we initiated a multi-center, global, randomized, double-blind, placebo-controlled Phase IIb clinical trial to evaluate the clinical efficacy endpoints as well as safety of aerosolized ALN-RSV01 in adult lung transplant patients naturally infected with RSV. The objective of this Phase IIb clinical trial is to repeat and extend the clinical results observed in the Phase IIa clinical trial described above. This trial is expected to enroll up to 76 adult lung transplant patients who will be randomized in a one-to-one drug to placebo ratio. The primary endpoint is reduction in the incidence of new or progressive BOS.

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We have formed collaborations with Cubist and Kyowa Hakko Kirin Co., Ltd., or Kyowa Hakko Kirin, for the development and commercialization of RNAi products for RSV. We have an agreement to jointly develop and commercialize certain RNAi products for RSV with Cubist in North America. Cubist has responsibility for developing and commercializing any such products in the rest of the world outside of Asia, and Kyowa Hakko Kirin has the responsibility for developing and commercializing any RNAi products for RSV in Asia. In November 2009, we and Cubist agreed that Alnylam would move forward with the development of ALN-RSV01, and together we would focus our collaboration and joint development efforts on ALN-RSV02, a second-generation compound, intended for use in pediatric patients. We and Cubist each bears one-half of the related development costs for ALN-RSV02. We are continuing to develop ALN-RSV01 for adult transplant patients at our sole discretion and expense. Cubist has the right to resume the collaboration on ALN-RSV01 in the future, which right may be exercised for a specified period of time following the completion of our Phase IIb clinical trial, subject to the payment by Cubist of an opt-in fee representing reimbursement of an agreed upon percentage of certain of our development expenses for ALN-RSV01.

In March 2009, we initiated a Phase I clinical trial for ALN-VSP, our second clinical program and our first systemically delivered RNAi therapeutic candidate. We are developing ALN-VSP for the treatment of liver cancers, including hepatocellular carcinoma, or HCC, and other solid tumors with liver involvement. This Phase I trial is a multi-center, open label, dose escalation study to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of intravenous ALN-VSP in up to approximately 55 patients with advanced solid tumors with liver involvement, including HCC. In June 2010, we reported preliminary results from this Phase I clinical trial. The results from the initial 19 patients in the first four dose cohorts demonstrate that ALN-VSP is well tolerated in most patients, and results from pharmacodynamic measurements provide preliminary evidence of biological activity. The majority of the patients treated had colorectal cancer, a primary tumor that often metastasizes to the liver. There were two mild acute infusion reactions; both patients had no further reactions with slowing of the infusion and stayed in the trial. At 0.7 mg/kg, a patient with advanced pancreatic neuroendocrine cancer with extensive involvement of the liver developed hepatic failure five days following the second dose and subsequently died; this was deemed possibly related to the study drug. Six additional patients treated at 0.7 mg/kg did not exhibit any evidence of hepatotoxicity. The trial has not yet reached a maximum tolerated dose and is continuing patient enrollment with dose escalation. Pharmacokinetic data showed that C_{max} (peak serum concentration of drug) and area under the curve were dose proportional with no evidence of drug accumulation. In addition, DCE-MRI results were suggestive of an anti-VEGF effect in the majority of treated patients. In 62% of evaluable liver tumors, there was a greater than 40% decline in K_{trans} (measure of blood flow), an effect that is comparable to what has been observed with other anti-VEGF drugs in solid tumors. Molecular and cellular analyses of biopsy samples are ongoing.

In July 2010, we initiated a Phase I clinical trial for ALN-TTR01, our second systemically delivered RNAi therapeutic candidate. We are developing ALN-TTR, which targets the transthyretin, or TTR, gene, for the treatment of TTR-mediated amyloidosis, or ATTR. ALN-TTR01 employs a first generation lipid nanoparticle, or LNP, formulation. The Phase I clinical trial for ALN-TTR01 is being conducted in Portugal, Sweden and the United Kingdom, and is a randomized, blinded, placebo-controlled dose escalation study designed to enroll approximately 28 ATTR patients. The primary objective is to evaluate the safety and tolerability of a single dose of intravenous ALN-TTR01. Secondary objectives include characterization of plasma and urine pharmacokinetics of ALN-TTR01 and assessment of pharmacodynamic activity based on measurements of circulating TTR serum levels. In parallel with this development, we are also advancing ALN-TTR02 utilizing second-generation LNPs.

In January 2010, we announced that we expect ALN-PCS, a systemically delivered RNAi therapeutic candidate for the treatment of hypercholesterolemia, to be our next clinical candidate. ALN-PCS targets a gene called proprotein convertase subtilisin/kexin type 9, or PCSK9. We are advancing ALN-PCS using second-generation LNPs for systemic delivery.

We are also working on a number of programs in pre-clinical development, including ALN-HTT, an RNAi therapeutic candidate targeting the huntingtin gene, for the treatment of Huntington's disease, or HD, which we are developing in collaboration with Medtronic, Inc., or Medtronic. In November 2010, we and Medtronic entered into an agreement with CHDI Foundation, Inc., or CHDI, under which CHDI has agreed to initially fund approximately 50% of the investigational new drug, or IND, application-enabling activities.

In addition to these development efforts, we are conducting research activities to discover RNAi therapeutics to treat various diseases including: viral hemorrhagic fever, including the Ebola virus, which can cause severe, often fatal infection and poses a potential biological safety risk and bioterrorism threat; Parkinson's disease, a progressive brain disease which is characterized by uncontrollable tremor and, in some cases, may result in dementia; and progressive multifocal leukoencephalopathy, or PML, which is a disease of the central nervous system caused by viral infection in immune compromised patients. We are also pursuing many other undisclosed internal pre-clinical programs.

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In addition to these programs, as part of our collaborations with F. Hoffmann-La Roche Ltd and certain of its affiliates, or Roche, and Takeda Pharmaceutical Company Limited, or Takeda, we are conducting research activities aimed at discovering RNAi therapeutics directed to a number of undisclosed targets.

We continue to work internally and with third-party collaborators to develop capabilities to deliver our RNAi therapeutics directly to specific sites of disease, such as the delivery of ALN-RSV to the lungs. We are also working to extend our capabilities to advance the development of RNAi therapeutics that are administered systemically by intravenous, subcutaneous or intramuscular approaches. We have made several of what we believe to be major advances relating to the delivery of RNAi therapeutics, both internally and together with our collaborators. We have numerous RNAi therapeutic delivery collaborations and intend to continue to collaborate with government, academic and corporate third parties to evaluate different delivery options.

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

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

We also seek opportunities to form new ventures in areas outside our core strategic focus. For example, during 2009, we presented new data regarding the application of RNAi technology to improve the manufacturing processes for biologics, including recombinant proteins and monoclonal antibodies. This initiative, which we are advancing in an internal effort referred to as Alnylam Biotherapeutics, has the potential to create new business opportunities. Additionally, in 2007, we and Isis established Regulus Therapeutics Inc., or Regulus, a company focused on the discovery, development and commercialization of microRNA therapeutics. Because microRNAs are believed to regulate whole networks of genes that can be involved in discrete disease processes, microRNA therapeutics represent a possible new approach to target the pathways of human disease. Given the broad applications for RNAi technology, we believe additional opportunities exist for new ventures.

In September 2010, as a result of the planned completion of the fifth and final year of the research program under our collaboration and license agreement with Novartis and our reduced need for service-based collaboration resources, our Board of Directors approved a corporate restructuring to focus our resources on our most promising programs and significantly reduce our cost structure. The corporate restructuring included implementing a reduction of our overall workforce by approximately 25%. We expect this reduction in personnel costs, along with other external costs, could result in a savings of approximately \$25.0 million in previously planned 2011 operating expenses. During the three months ended September 30, 2010, we recorded \$2.2 million in operating expenses under the restructuring, including employee severance, benefits and related costs. These expenses are expected to be substantially paid by the end of the first half of 2011.

Alnylam commenced operations in June 2002. We have focused our efforts since inception primarily on business planning, research and development, acquiring, filing and expanding intellectual property rights, recruiting management and technical staff, and raising capital. Since our inception, we have generated significant losses. As of

September 30, 2010, we had an accumulated deficit of \$336.4 million. Through September 30, 2010, we have funded our operations primarily through the net proceeds from the sale of equity securities and payments we have received under strategic alliances. Through September 30, 2010, a substantial portion of our total net revenues have been collaboration revenues derived from our strategic alliances with Roche, Takeda and Novartis, and from the United States government in connection with our development of treatments for hemorrhagic fever viruses, including Ebola. We expect our revenues to continue to be derived primarily from new and existing strategic alliances, government and foundation funding, and license fee revenues.

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We currently have programs focused in a number of therapeutic areas. However, we are unable to predict when, if ever, we will successfully develop or be able to commence sales of any product. We have never achieved profitability on an annual basis and we expect to incur additional losses over the next several years. We expect our net losses to continue due primarily to research and development activities relating to our drug development programs, collaborations and other general corporate activities. We anticipate that our operating results will fluctuate for the foreseeable future. Therefore, period-to-period comparisons should not be relied upon as predictive of the results in future periods. Our sources of potential funding for the next several years are expected to be derived primarily from payments under new and existing strategic alliances, which may include license and other fees, funded research and development payments and milestone payments, government and foundation funding, and proceeds from the sale of equity.

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. Our most advanced program is focused on the treatment of RSV infection and is in Phase II clinical trials. In March 2009, we initiated a Phase I clinical trial for ALN-VSP, our second clinical program and our first systemically delivered RNAi therapeutic candidate for the treatment of primary and secondary liver cancer. In July 2010, we initiated a Phase I clinical trial of ALN-TTR01, our second systemically delivered RNAi therapeutic candidate, in ATTR patients. Both ALN-VSP and ALN-TTR01 employ a first generation LNP formulation. In parallel, we are also advancing ALN-TTR02 utilizing second-generation LNPs. In January 2010, we announced that we expect ALN-PCS, a systemically delivered RNAi therapeutic candidate for the treatment of hypercholesterolemia, to be our next clinical candidate. We are advancing ALN-PCS using second-generation LNPs for systemic delivery. We also have a development program focused on the treatment of HD. In addition, we have discovery programs to develop RNAi therapeutics for the treatment of a broad range of diseases, such as viral hemorrhagic fever, including the Ebola virus, Parkinson's disease, PML and other undisclosed programs, as well as several other diseases that are the subject of our strategic alliances. We are working internally and with third-party collaborators to develop capabilities to deliver our RNAi therapeutics both directly to the specific sites of disease and systemically, and we intend to continue to collaborate with government, academic and corporate third parties to evaluate different delivery options.

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 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 collaborative, 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 of any products that we may develop; and

the effect of competing technological and market developments.

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Any failure to complete any stage of the development of any potential products in a timely manner could have a material adverse effect on our operations, financial position and liquidity. A discussion of some of the risks and uncertainties associated with completing our projects on schedule, or at all, and the potential consequences of failing to do so, are set forth in Part II, Item 1A below under the heading Risk Factors.

Strategic Alliances

A significant component of our business plan is to enter into strategic alliances and collaborations with pharmaceutical and biotechnology companies, academic institutions, research foundations and others, as appropriate, to gain access to funding, capabilities, technical resources and intellectual property to further our development efforts and to generate revenues. Our collaboration strategy is to form (1) non-exclusive platform alliances where our collaborators obtain access to our capabilities and intellectual property to develop their own RNAi therapeutic products; and (2) 50-50 co-development and/or worldwide or specific geographic partnerships on specific RNAi therapeutic programs. We have entered into broad, non-exclusive platform license agreements with Roche and Takeda, under which we are also collaborating with each of Roche and Takeda on RNAi drug discovery for one or more disease targets. We are pursuing 50-50 co-development programs with Cubist and Medtronic for the development and commercialization of ALN-RSV02 and ALN-HTT, respectively. In addition, we have entered into a product alliance with Kyowa Hakko Kirin for the development and commercialization of ALN-RSV in territories not covered by the Cubist agreement, which include Japan and other markets in Asia. We also have discovery and development alliances with Isis and Biogen Idec.

We also seek opportunities to form new ventures in areas outside our core strategic focus. For example, during 2009, we established Alnylam Biotherapeutics, an internal effort regarding the application of RNAi technology to improve the manufacturing processes for biologics, an approach that has the potential to create new business opportunities. This initiative is focused on applying RNAi technologies to the biologics marketplace, which includes recombinant proteins and monoclonal antibodies. In addition, during 2007, we formed Regulus, together with Isis, to capitalize on our technology and intellectual property in the field of microRNA therapeutics. Given the broad applications for RNAi technology, we believe additional opportunities exist for new ventures.

To generate revenues from our intellectual property rights, we grant licenses to biotechnology companies under our InterfeRx program for the development and commercialization of RNAi therapeutics for specified targets in which we have no direct strategic interest. We also license key aspects of our intellectual property to companies active in the research products and services market, which includes the manufacture and sale of reagents. Our InterfeRx and research product licenses aim to generate modest near-term revenues that we can re-invest in the development of our proprietary RNAi therapeutics pipeline. As of September 30, 2010, we had granted such licenses, on both an exclusive and non-exclusive basis, to approximately 20 companies.

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

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

Novartis Alliance. In April 2010, pursuant to terms of the investor rights agreement between us and Novartis, Novartis purchased 55,223 shares of our common stock, at a purchase price of \$17.99 per share, resulting in an aggregate payment to us of \$1.0 million. Under the investor rights agreement, we granted Novartis rights to acquire additional equity securities such that Novartis would be able to maintain its ownership percentage, which following this purchase was approximately 13.4% of our outstanding common stock.

Our collaboration and license agreement with Novartis had an initial term of three years, with an option for two additional one-year extensions that were exercised by Novartis. In October 2010, the fifth and final year of the research program was substantially completed in accordance with the terms of the collaboration and license agreement, subject to certain surviving rights and obligations. In September 2010, Novartis exercised its right under the collaboration and license agreement to select 31 designated gene targets, for which Novartis has exclusive rights to discover, develop and commercialize RNAi therapeutic products using our intellectual property and technology. Under the terms of the collaboration and license agreement, for any RNAi therapeutic products

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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. Novartis also notified us that it had declined to exercise its option for a broad, non-exclusive license under the terms of the collaboration and license agreement.

CHDI Alliance. In November 2010, we, Medtronic and CHDI formed a collaboration to advance ALN-HTT, a novel drug-device combination for the treatment of HD. CHDI is a not-for-profit virtual biotech company that is exclusively dedicated to rapidly discovering and developing therapies that slow the progression of HD. We and Medtronic have been working collaboratively on advancing ALN-HTT for the treatment of HD under a collaboration agreement, originally executed in 2005 and amended and restated in 2007.

Under this new collaboration, CHDI has agreed to initially fund approximately 50% of the IND application-enabling activities which represents over \$10.0 million in potential funding. The Medtronic agreement will remain as a 50-50 partnership in the United States. With respect to the initial product development program focused on HD, each of us and Medtronic is funding 50% of the development efforts for the United States. Medtronic will commercialize any resulting product consisting of the RNAi compound and delivery device. In the United States, we have the opportunity to invest in clinical development through product launch in return for a proportional share of the profits. In Europe, Medtronic is solely responsible for development and commercialization, and we are eligible to receive milestones and royalties on product sales, if any.

Isis Alliance. In April 2009, we and Isis established a collaborative effort focused on the development of single-stranded RNAi, or ssRNAi, technology, pursuant to which we obtained from Isis a co-exclusive, worldwide license to Isis current and future patents and patent applications relating to chemistry and RNA-targeting mechanisms to research, develop and commercialize ssRNAi products. Under the terms of the amended and restated Isis agreement, we are obligated to pay Isis certain license fees, including \$10.0 million payable if and when we determine to move forward with the collaborative effort, or if and when *in vivo* efficacy in rodents is demonstrated, if sooner. We are also obligated to fund certain research activities at a minimum of \$3.0 million each year for three years with research and development activities conducted by both us and Isis. We and Isis have mutually agreed to extend our unilateral right to terminate the ssRNAi research program from September 30, 2010 into the fourth quarter of 2010. During this extension, our obligation to provide research funding has been suspended. In the event that we terminate the research program, any licenses to ssRNAi products granted by Isis to us under the amended and restated agreement, and any obligation thereunder by us to provide additional research funding or pay additional license fees, milestone payments, royalties or sublicense payments to Isis for such ssRNAi products, would also terminate.

Delivery Initiatives

We are working internally and with third-party collaborators to extend our capabilities in developing technology to achieve effective and safe delivery of RNAi therapeutics to a broad spectrum of organ and tissue types. In connection with these efforts, we have entered into a number of agreements to evaluate and gain access to certain delivery technologies. In some instances, we are also providing funding to support the advancement of these delivery technologies. We believe that we have made considerable progress in developing our product platform. We have made several of what we believe to be major advances relating to the delivery of RNAi therapeutics, both internally and together with our collaborators. The first relates to the discovery of new LNP compositions that provide dramatic improvements in the potency of gene silencing as compared to first generation LNPs. Additionally, we believe we have discovered an important *in vivo* mechanism for delivery relating to the role of endogenous apolipoprotein E, or ApoE, a plasma protein involved in lipoprotein metabolism, in the delivery of certain LNPs into the cytoplasm of certain cells. The latter discovery has allowed the specific targeting of LNPs and allows the possibility of delivery beyond the liver.

In May 2007, we entered into an agreement with the David H. Koch Institute for Integrative Cancer Research at MIT, under which we are sponsoring an exclusive five-year research program focused on the delivery of RNAi therapeutics. In addition, during 2007, we obtained an exclusive worldwide license to the liposomal delivery formulation technology of Tekmira for the discovery, development and commercialization of LNP formulations for the delivery of RNAi therapeutics and a non-exclusive worldwide license to certain liposomal delivery formulation technology of Protiva Biotherapeutics Inc., or Protiva, for the discovery, development and commercialization of

certain LNP formulations for the delivery of RNAi therapeutics. In May 2008, Tekmira acquired Protiva. In connection with this acquisition, we entered into new agreements with Tekmira and Protiva, which provide us access to key existing and future technology and intellectual property for the systemic delivery of RNAi therapeutics with liposomal delivery technologies. Under these agreements, we continue to have exclusive rights to the Semple (U.S. Patent No. 6,858,225) and Wheeler (U.S. Patent Nos. 5,976,567 and 6,815,432) patents for RNAi, which we believe are critical for the use of LNP delivery technology. In July 2009, we and Tekmira agreed to jointly participate in a new research collaboration with scientists at UBC and AICana focused on the discovery of novel lipids for use in LNPs for the systemic delivery of RNAi therapeutics. We are funding the collaborative research over a two-year period, and the work is being conducted by our scientists together with scientists at UBC and AICana. We will receive exclusive rights to all new inventions as well as sole rights to sublicense any resulting intellectual property to our current and future collaborators. Tekmira will receive rights to use new inventions for their own RNAi therapeutic programs that are licensed under our InterfeRx program. In October 2010, we provided Tekmira with an additional InterfeRx license in connection with their research program directed towards the Ebola virus, bringing the total number of InterfeRx licenses granted to Tekmira up to eight.

We are developing ALN-VSP, a systemically delivered RNAi therapeutic candidate, for the treatment of primary and secondary liver cancer. ALN-VSP contains two siRNAs formulated using the first generation LNP formulation known as stable nucleic acid-lipid particles, or SNALP, developed in collaboration with Tekmira. We also have rights to use SNALP technology in the advancement of our other systemically delivered RNAi therapeutic programs, and are advancing ALN-TTR01, for the treatment of ATTR, utilizing a first generation SNALP formulation. In parallel with ALN-TTR01, we are advancing ALN-TTR02 utilizing second-generation LNPs. In addition, we have published pre-clinical results from development programs for other systemically delivered RNAi therapeutic candidates, including ALN-PCS, for the treatment of hypercholesterolemia, which we recently identified as our next clinical candidate. We are advancing ALN-PCS using second-generation LNPs for systemic delivery.

We are pursuing additional approaches for delivery that include other LNP formulations, mimetic lipoprotein particles, or MLPs, siRNA conjugation strategies and ssRNAi, among others. In addition, we have other RNAi therapeutic delivery collaborations and intend to continue to collaborate with government, academic and corporate third parties to evaluate and gain access to different delivery technologies.

Alnylam Biotherapeutics

During 2009, we presented new data regarding the application of RNAi technology to improve the manufacturing processes

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for biologics, including recombinant proteins and monoclonal antibodies. This initiative, which we are advancing in an internal effort referred to as Alnylam Biotherapeutics, has 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. As Alnylam Biotherapeutics advances the technology, it plans to seek collaborations with established biologic manufacturers, selling licenses, products and services.

microRNA Therapeutics

Regulus. In September 2007, we and Isis established Regulus, a company focused on the discovery, development and commercialization of microRNA therapeutics. Regulus combines our and Isis technologies, know-how and intellectual property relating to microRNA therapeutics. Since microRNAs are believed to regulate the expression of broad networks of genes and biological pathways, microRNA therapeutics define a new and potentially high-impact strategy to target multiple points on disease pathways.

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. In addition, we made an initial cash contribution to Regulus of \$10.0 million, resulting in us and Isis making initial capital contributions to Regulus of approximately equal aggregate value. In addition, in March 2009, we and Isis each purchased \$10.0 million of Series A preferred stock of Regulus. As of September 30, 2010, we and Isis owned approximately 49% and 51%, respectively, of Regulus and there were no other third-party investors in Regulus. Regulus continues to operate as an independent company with a separate board of directors, scientific advisory board and management team, some of whom have options to purchase common stock of Regulus. Members of the board of directors of Regulus who are our employees or Isis employees are not eligible to receive options to purchase Regulus common stock.

Regulus most advanced program, which is in pre-clinical research, is a microRNA therapeutic candidate that targets miR-122. miR-122 is a liver-expressed microRNA that has been shown to be a critical endogenous host factor for the replication of hepatitis C virus, or HCV, infection, and anti-miRs targeting miR-122 have been shown to block HCV infection. HCV infection is a significant disease worldwide, for which emerging therapies target viral genes and, therefore, are prone to viral resistance. Regulus is also pursuing a program that targets miR-21. Pre-clinical studies by Regulus and collaborators have shown that miR-21 is implicated in several therapeutic areas, including heart failure and fibrosis. In addition to these programs, Regulus is also actively exploring additional areas for development of microRNA therapeutics, including cancer, other viral diseases, metabolic disorders and inflammatory diseases.

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

In February 2010, Regulus and GSK established a new collaboration to develop and commercialize microRNA therapeutics targeting miR-122 in all fields, with the treatment of HCV infection as the lead indication. Under the terms of this new collaboration, Regulus received \$8.0 million in upfront payments from GSK, including a \$3.0 million license fee and a loan of \$5.0 million (guaranteed by us and Isis) that will convert into Regulus common stock under certain specified circumstances. Consistent with the original GSK alliance, Regulus could be eligible to

receive development, regulatory and sales milestone payments, as well as royalty payments on worldwide sales of products resulting from the alliance, if any, as Regulus and GSK advance microRNA therapeutics targeting miR-122.

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In June 2010, Regulus entered into a global, strategic alliance with sanofi-aventis to discover, develop and commercialize microRNA therapeutics on up to four microRNA targets. Under the terms of this new alliance, Regulus received \$25.0 million in upfront fees and is entitled to annual research support for three years with the option to extend research support for two additional years. As part of this alliance, in October 2010, sanofi-aventis made a \$10.0 million equity investment in Regulus, resulting in sanofi-aventis owning approximately 9% of Regulus. Following this investment, we and Isis own approximately 45% and 46%, respectively, of Regulus.

In addition, Regulus is eligible to receive royalties on microRNA therapeutic products commercialized by sanofi-aventis, if any. Sanofi-aventis will support 100% of the costs of clinical development and commercialization of each program. The alliance will initially focus on the therapeutic area of fibrosis. Regulus and sanofi-aventis will collaborate on up to four microRNA targets, including Regulus lead fibrosis program targeting miR-21. Sanofi-aventis also received an option for a broader technology alliance with Regulus that provides Regulus certain rights to participate in development and commercialization of resulting products. If exercised, this option is worth up to an additional \$50.0 million to Regulus. In addition, we and Isis are each eligible to receive 7.5% of all potential milestone payments, in addition to royalties on product sales, if any. During the nine months ended September 30, 2010, we recognized related-party revenues of \$1.9 million from Regulus in our condensed consolidated statements of operations in connection with this alliance, representing 7.5% of the \$25.0 million upfront payment from sanofi-aventis to Regulus.

Intellectual Property

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

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

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

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

In June 2009, we joined with Max-Planck-Gesellschaft Zur Forderung Der Wissenschaften E.V. and Max-Planck-Innovation GmbH, collectively, Max Planck, in taking legal action against Whitehead, MIT and the Board of Trustees of the University of Massachusetts, or UMass. The complaint, initially filed in the Suffolk County Superior Court in Boston, Massachusetts and subsequently removed to the U.S. District Court for the District of Massachusetts, alleges, among other things, that the defendants have improperly prosecuted the so-called Tuschl I patent applications and wrongfully incorporated inventions covered by the so-called Tuschl II patent applications into the Tuschl I patent applications, thereby potentially damaging the value of inventions reflected in the Tuschl I and Tuschl II patent applications. In the field of RNAi therapeutics, we are the exclusive licensee of the Tuschl I patent applications from Max Planck, MIT and Whitehead, and of the Tuschl II patent applications from Max Planck.

The complaint seeks, among other things, a declaratory judgment regarding the prosecution of the Tuschl I patent family and unspecified monetary damages. In August 2009, Whitehead and UMass filed counterclaims against us and

Max Planck, including for breach of contract. In January 2010, we and Max Planck filed an amended complaint expanding upon the allegations in the original complaint. We currently expect a jury trial to start in early 2011. In February 2010, we and Max Planck released MIT from any claims seeking monetary damages, and MIT has stipulated that it will be bound by any declaratory, injunctive, or equitable relief granted by the court.

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In addition, in September 2009, the U.S. Patent and Trademark Office, or USPTO, granted Max Planck's petition to revoke power of attorney in connection with the prosecution of the Tuschl I patent application. This action prevents the defendants from filing any papers with the USPTO in connection with further prosecution of the Tuschl I patent application without the agreement of Max Planck. Whitehead's petition to overturn this ruling was denied. Prosecution before the USPTO for both the Tuschl I and II pending patent applications was suspended pursuant to a standstill agreement. This agreement expired on September 15, 2010, and Max Planck, MIT, Whitehead and UMass agreed to file several continuation applications in the Tuschl I patent family to preserve their rights and maintain the status quo for these applications. Max Planck also filed a continuation application in the Tuschl II patent family.

Although we, along with Max Planck, are vigorously asserting our rights in this case, litigation is subject to inherent uncertainty and a court could ultimately rule against us and Max Planck. In addition, litigation is costly and may divert the attention of our management and other resources that would otherwise be engaged in running our business.

In July 2009, we announced that we will contribute more than 1,500 patents or pending patent applications in our RNAi technology patent estate to the Pool for Open Innovation against Neglected Tropical Diseases, a patent pool established by GSK in March 2009. We were the first company to add its patents to the approximately 800 patent filings GSK provided to the pool. The patent pool was formed to aid in the discovery and development of new medicines for the treatment of 16 neglected tropical diseases, or NTDs, as defined by the United States Food and Drug Administration, or FDA, in the world's least developed countries. BIO Ventures for Global Health, or BVGH, has been appointed to administer the patent pool. In 2010, MIT became the first academic institution to contribute intellectual property to the patent pool. In addition, in 2010, South Africa's Technology Innovation Agency, or TIA, became the first government agency to join in the patent pool. TIA intends to use intellectual property and know-how from the patent pool to accelerate its efforts to grow the South African biotechnology sector and enhance the quality of life of those affected by NTDs. Emory Institute for Drug Development and iThemba Pharmaceuticals also joined the patent pool in 2010 to access its know-how, experience and intellectual property to accelerate their drug discovery initiatives for NTDs, and the Medicines for Malaria Venture joined as the first product development partnership to contribute intellectual property to the patent pool.

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, 2009, which we filed with the SEC on February 26, 2010.

Results of Operations

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

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2010	2009	2010	2009
Net revenues	\$27,668	\$24,249	\$ 78,849	\$ 73,907
Operating expenses	36,396	33,899	110,509	113,949
Loss from operations	(8,728)	(9,650)	(31,660)	(40,042)
Net loss	\$ (9,630)	\$ (9,208)	\$ (36,585)	\$ (39,799)

Revenues

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

	Three Months Ended		Nine Months Ended	
	September 30,		September 30,	
	2010	2009	2010	2009
Roche	\$ 13,995	\$ 13,844	\$ 41,983	\$ 41,639

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Takeda	5,556	5,438	16,479	16,274
Novartis	3,984	2,182	8,957	7,104
Government contract	1,008	1,410	4,095	5,144
Other research collaborator	821	945	4,338	2,772
InterfeRx program, research reagent license and other	2,304	430	2,997	974
Total net revenues from research collaborators	\$ 27,668	\$ 24,249	\$ 78,849	\$ 73,907

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The increase in Novartis revenues for the three and nine months ended September 30, 2010 as compared to the three and nine months ended September 30, 2009 was due primarily to an increase in the number of resources allocated to the Novartis collaboration. The increase in InterfeRx program, research reagent license and other revenues for the three and nine months ended September 30, 2010 as compared to the three and nine months ended September 30, 2009 was primarily a result of progress and milestones achieved related to our InterfeRx and other programs. In addition, other research collaborator revenues increased for the nine months ended September 30, 2010 as compared to the nine months ended September 30, 2009 primarily as a result of the \$1.9 million sublicense fee recognized in connection with Regulus June 2010 alliance with sanofi-aventis, representing 7.5% of the \$25.0 million upfront payment from sanofi-aventis to Regulus.

Partially offsetting these increases, government contract revenues decreased for the three and nine months ended September 30, 2010 as compared to the three and nine months ended September 30, 2009, in part as a result of a decrease in the research and development activities related to our contract with the NIAID. This contract was originally expected to be completed in September 2010. We and the NIAID have agreed to a no-cost extension of the contract through December 2010 during which time the funds remaining under the contract will be available to us.

In September 2010, Novartis exercised its right under the collaboration and license agreement to select 31 designated gene targets, for which Novartis has exclusive rights to discover, develop and commercialize RNAi therapeutic products using our intellectual property and technology. Novartis also notified us that it had declined to exercise its non-exclusive option to integrate into its operations our fundamental and chemistry intellectual property under the terms of the collaboration and license agreement, known as the integration option. If Novartis had elected to exercise the integration option, Novartis would have been required to make additional payments to us totaling \$100.0 million. In October 2010, the fifth and final year of the research program was substantially completed under the Novartis collaboration and license agreement, and a significant portion of the related Novartis revenues will end in the fourth quarter of 2010.

Total deferred revenue of \$230.9 million at September 30, 2010 consists of payments we have received from collaborators, primarily Roche, Takeda, Kyowa Hakko Kirin and Cubist, but have not yet recognized pursuant to our revenue recognition policies.

Due to the planned completion of the Novartis research collaboration and the expected completion of our contract with the NIAID, we expect our net revenues to decrease significantly beginning in the fourth quarter of 2010. Partially offsetting this decrease, we will recognize \$2.0 million of revenues in the fourth quarter of 2010 in connection with an award under the Federal government's Qualifying Therapeutic Discovery Project Program. For the foreseeable future, we expect our revenues to continue to be derived primarily from our alliances with Roche, Takeda and Cubist, as well as other strategic alliances, collaborations, foundation funding, government contracts and licensing activities.

Operating expenses

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

	Three Months	% of Total	Three Months	% of Total	Increase (Decrease)	
	Ended September 30, 2010	Operating Expenses	Ended September 30, 2009	Operating Expenses	\$	%
Research and development	\$ 27,468	75%	\$ 23,219	68%	\$ 4,249	18%
General and administrative	8,928	25%	10,680	32%	(1,752)	(16)%
Total operating expenses	\$ 36,396	100%	\$ 33,899	100%	\$ 2,497	7%

	Nine Months	% of Total	Nine Months	% of Total	Increase (Decrease)	
	Ended September 30, 2010	Operating Expenses	Ended September 30, 2009	Operating Expenses	\$	%
Research and development	\$ 80,304	73%	\$ 87,155	76%	\$ (6,851)	(8)%
General and administrative	30,205	27%	26,794	24%	3,411	13%
Total operating expenses	\$ 110,509	100%	\$ 113,949	100%	\$ (3,440)	(3)%

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Research and development. The tables below 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, 2010	% of Expense Category	Three Months Ended September 30, 2009	% of Expense Category	Increase (Decrease) \$ %	
Research and development						
Compensation and related	\$ 6,121	22%	\$ 5,350	23%	\$ 771	14%
External services	5,392	20%	5,263	23%	129	2%
Clinical trial and manufacturing	4,974	18%	3,293	14%	1,681	51%
Facilities-related	3,049	11%	2,861	12%	188	7%
Non-cash stock-based compensation	2,725	10%	3,128	13%	(403)	(13)%
Lab supplies and materials	1,982	7%	1,913	8%	69	4%
Restructuring	1,863	7%			1,863	100%
License fees	667	2%	814	4%	(147)	(18)%
Other	695	3%	597	3%	98	16%
Total research and development expenses	\$ 27,468	100%	\$ 23,219	100%	\$ 4,249	18%

Research and development expenses increased during the three months ended September 30, 2010 as compared to the three months ended September 30, 2009 due primarily to employee severance, benefits and related costs incurred in connection with our corporate restructuring, which was implemented at the end of September 2010 and included an approximate 25% workforce reduction. Clinical trial and manufacturing expenses increased during the three months ended September 30, 2010 as compared to the three months ended September 30, 2009 due primarily to higher clinical trial and manufacturing costs as we continue to advance our ALN-RSV, ALN-VSP and ALN-TTR programs. In addition, compensation and related expenses increased during the three months ended September 30, 2010 as compared to the three months ended September 30, 2009 due to higher average research and development headcount to support our technology platform and expanding product pipeline.

We expect to continue to devote a substantial portion of our resources to research and development expenses as we continue development of our and our collaborators' product candidates and focus on continuing to develop drug delivery-related technologies. As a result of our corporate restructuring, we expect that compensation and related research and development expenses will decrease during the remainder of 2010.

A significant portion of our research and development costs are not tracked by project as they benefit multiple projects or our technology platform and because our most-advanced programs are in the early stages of clinical development. However, our collaboration agreements contain cost-sharing arrangements whereby certain costs incurred under the project are reimbursed. Costs reimbursed under the agreements typically include certain direct external costs and a negotiated full-time equivalent labor rate for the actual time worked on the project. In addition, we are reimbursed under our 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	Nine Months
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	Ended September 30, 2010	% of Expense Category	Ended September 30, 2009	% of Expense Category	Increase (Decrease) \$ %	
Research and development						
Compensation and related	\$ 18,439	23%	\$ 16,220	19%	\$ 2,219	14%
External services	15,879	20%	16,411	19%	(532)	(3)%
Clinical trial and manufacturing	15,249	19%	14,692	17%	557	4%
Non-cash stock-based compensation	9,200	12%	9,410	11%	(210)	(2)%
Facilities-related	8,967	11%	8,809	10%	158	2%
Lab supplies and materials	6,250	8%	6,069	7%	181	3%
Restructuring	1,863	2%			1,863	100%
License fees	1,848	2%	13,497	15%	(11,649)	(86)%
Other	2,609	3%	2,047	2%	562	27%
Total research and development expenses	\$ 80,304	100%	\$ 87,155	100%	\$ (6,851)	8%

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Research and development expenses decreased during the nine months ended September 30, 2010 as compared to the nine months ended September 30, 2009 due primarily to license fees paid to Isis in connection with our ssRNAi program under the amended and restated Isis agreement entered into in April 2009, as well as higher license fees payable to certain entities during the nine months ended September 30, 2009, primarily Isis, as a result of the Cubist alliance. This decrease was partially offset by restructuring expenses related to employee severance, benefits and related costs incurred in connection with our corporate restructuring, which was implemented at the end of September 2010 and included an approximate 25% workforce reduction. In addition, there was an increase in compensation and related expenses during the nine months ended September 30, 2010 as compared to the nine months ended September 30, 2009 due to higher average research and development headcount to support our technology platform and expanding product pipeline.

General and administrative. The tables below 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, 2010	% of Expense Category	Three Months Ended September 30, 2009	% of Expense Category	Increase (Decrease) \$ %	
General and administrative						
Consulting and professional services	\$ 4,119	46%	\$ 5,893	55%	\$ (1,774)	(30)%
Non-cash stock-based compensation	1,787	20%	2,110	20%	(323)	(15)%
Compensation and related	1,543	17%	1,429	13%	114	8%
Facilities-related	609	7%	682	6%	(73)	(11)%
Restructuring	330	4%			330	100%
Insurance	188	2%	181	2%	7	4%
Other	352	4%	385	4%	(33)	(9)%
Total general and administrative expenses	\$ 8,928	100%	\$ 10,680	100%	\$ (1,752)	(16)%

The decrease in general and administrative expenses during the three months ended September 30, 2010 as compared to the three months ended September 30, 2009 was due primarily to lower consulting and professional services expenses related to business activities, primarily legal activities, a description of which is set forth below under Part II, Item 1 Legal Proceedings. As a result of our corporate restructuring, we expect that general and administrative expenses, excluding expenses associated with legal activities, will decrease slightly during the remainder of 2010.

	Nine Months Ended September 30, 2010	% of Expense Category	Nine Months Ended September 30, 2009	% of Expense Category	Increase (Decrease) \$ %	
General and administrative						
	\$ 15,755	52%	\$ 11,493	43%	\$ 4,262	37%

Consulting and professional services						
Non-cash stock-based compensation	5,706	19%	6,377	24%	(671)	(11)%
Compensation and related	4,767	16%	4,907	18%	(140)	(3)%
Facilities-related	1,795	6%	2,055	8%	(260)	(13)%
Insurance	564	2%	536	2%	28	5%
Restructuring	330	1%			330	100%
Other	1,288	4%	1,426	5%	(138)	(10)%
Total general and administrative expenses	\$ 30,205	100%	\$ 26,794	100%	\$ 3,411	13%

The increase in general and administrative expenses during the nine months ended September 30, 2010 as compared to the nine months ended September 30, 2009 was due primarily to higher consulting and professional services expenses related to business activities, primarily legal activities, a description of which is set forth below under Part II, Item 1 Legal Proceedings.

Table of Contents***Other income (expense)***

We incurred \$1.2 million and \$6.7 million equity in loss of joint venture (Regulus Therapeutics Inc.) for the three and nine months ended September 30, 2010, respectively, as compared to \$1.1 million and \$3.4 million equity in loss of joint venture (Regulus Therapeutics Inc.) for the three and nine months ended September 30, 2009, respectively, related to our approximate 49% share of the net losses incurred by Regulus. The increase in Regulus net loss for the three and nine months ended September 30, 2010 was due primarily to our 49% share of \$3.8 million of sublicense fees payable to Isis and us in connection with the strategic alliance formed by Regulus and sanofi-aventis in June 2010. In October 2010, sanofi-aventis made a \$10.0 million equity investment in Regulus, resulting in sanofi-aventis owning approximately 9% of Regulus. Following this investment, we and Isis own approximately 45% and 46%, respectively, of Regulus.

Interest income was \$0.6 million and \$1.8 million for the three and nine months ended September 30, 2010, respectively, as compared to \$1.0 million and \$4.5 million for the three and nine months ended September 30, 2009, respectively. The decrease was due primarily to lower average interest rates as well as lower average cash, cash equivalent and marketable securities balances.

Provision for income taxes was \$0.3 million and \$0.1 million for the three and nine months ended September 30, 2010, respectively, as compared to a benefit from income taxes of \$0.6 million and a provision for income taxes of \$1.0 million for the three and nine months ended September 30, 2009, respectively. The provision for income taxes for the nine months ended September 30, 2009 was due primarily to taxable income in 2009 as a result of our alliances with Roche and Takeda.

Liquidity and Capital Resources

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

	Nine Months Ended September 30,	
	2010	2009
Net loss	\$ (36,585)	\$ (39,799)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities	25,548	24,461
Changes in operating assets and liabilities	(52,916)	(39,938)
Net cash used in operating activities	(63,953)	(55,276)
Net cash used in investing activities	(29,741)	(41,186)
Net cash provided by financing activities	3,136	2,874
Effect of exchange rate on cash	(29)	(117)
Net decrease in cash and cash equivalents	(90,587)	(93,705)
Cash and cash equivalents, beginning of period	137,468	191,792
Cash and cash equivalents, end of period	\$ 46,881	\$ 98,087

Since we commenced operations in 2002, we have generated significant losses. As of September 30, 2010, we had an accumulated deficit of \$336.4 million. As of September 30, 2010, we had cash, cash equivalents and marketable securities of \$371.9 million, compared to cash, cash equivalents and marketable securities of \$435.3 million as of December 31, 2009. We invest primarily in cash equivalents, U.S. government and municipal obligations, high-grade corporate notes and commercial paper. Our investment objectives are, primarily, to assure liquidity and preservation of capital and, secondarily, to obtain investment income. All of our investments in debt securities are recorded at fair value and are available-for-sale. Fair value is determined based on quoted market prices and models using observable data inputs. We have not recorded any impairment charges to our fixed income marketable securities during the nine months ended September 30, 2010.

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, 2010, net cash used in operating activities of \$64.0 million was due primarily to our net loss and other changes in our working capital. We had a decrease in deferred revenue of \$40.9 million for the nine months ended September 30, 2010, as well as a decrease in income taxes payable of \$5.5 million. Cash used in operating activities is adjusted for non-cash items to reconcile net loss to net cash used in or provided by operating activities. These non-cash adjustments consist primarily of stock-based compensation, equity in loss of joint venture (Regulus Therapeutics Inc.), and depreciation and amortization.

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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, 2010, net cash used in investing activities of \$29.7 million resulted primarily from net purchases of marketable securities of \$26.1 million and purchases of property and equipment of \$3.6 million. For the nine months ended September 30, 2009, net cash used in investing activities of \$41.2 million resulted primarily from net purchases of marketable securities of \$33.7 million, an additional \$10.0 million investment in Regulus, and purchases of property and equipment of \$3.7 million related to our Cambridge facility. Offsetting these amounts for the nine months ended September 30, 2009 was a decrease in restricted cash of \$6.2 million, resulting from the release of letters of credit in connection with the amendment of our facility lease and the termination of our sublease agreement.

Financing activities

For the nine months ended September 30, 2010, net cash provided by financing activities of \$3.1 million was due to proceeds of \$1.0 million from our issuance of common stock to Novartis in April 2010, as well as proceeds from the issuance of common stock in connection with stock option exercises. For the nine months ended September 30, 2009, net cash provided by financing activities of \$2.9 million was due primarily to proceeds of \$1.2 million from our issuance of common stock to Novartis in May 2009, as well as proceeds from the issuance of common stock in connection with stock option exercises.

During the current downturn in global financial markets, some companies have experienced difficulties accessing their cash equivalents, investment securities and raising capital generally, which have had a material adverse impact on their liquidity. In addition, the current economic downturn has diminished the availability of capital and may limit our ability to access these markets to obtain financing in the future. Based on our current operating plan, we believe that our existing cash, cash equivalents and fixed income marketable securities, for which we have not recognized any impairment charges, together with the cash we expect to generate under our current alliances, including our Novartis, Roche, Takeda and Cubist alliances, will be sufficient to fund our planned operations for at least the next several years, during which time we expect to further the development of our product candidates, conduct clinical trials, extend the capabilities of our technology platform, including through new business initiatives, and continue to prosecute patent applications and otherwise build and maintain our patent portfolio. However, we may require significant additional funds earlier than we currently expect in order to develop, conduct clinical trials for and commercialize any product candidates.

In the longer term, we may seek additional funding through additional collaborative arrangements and public or private financings. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. For example, if we raise additional funds by issuing equity securities, further dilution to our existing stockholders may result. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail one or more of our research or development programs. We also could be required to seek funds through arrangements with collaborators or others that may require us to relinquish rights to some of our technologies or product candidates that we would otherwise pursue.

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;

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

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

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

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

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

the costs associated with legal activities arising in the course of our business activities;

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, 2009. In May 2010, we amended our lease for our Cambridge, Massachusetts facility to lease an additional 34,000 square feet, effective as of October 1, 2010. We lease a total of approximately 129,000 square feet of office and laboratory space at the premises under the amended lease. The term of the amended lease expires in September 2016. As a result, our operating lease obligations through 2016 increased by an aggregate of \$8.9 million as a result of the amended lease, partially offset by future sublease payments to us of \$1.7 million, resulting in a net increase of \$7.2 million. We have separately agreed to sublease the first floor of the premises through the end of 2011.

Recent Accounting Pronouncements

In April 2010, the Financial Accounting Standards Board, or FASB, issued a new accounting standard, which provides guidance in applying the milestone method of revenue recognition to research or development arrangements. Under this guidance management may recognize revenue contingent upon the achievement of a milestone in the period in which the milestone is achieved only if the milestone meets all the criteria within the guidance to be considered substantive. This standard is effective on a prospective basis for research and development milestones achieved in fiscal years beginning on or after June 15, 2010. We are currently evaluating the potential impact of this accounting standard on our condensed consolidated financial statements, however we do not believe it will have a significant impact.

In October 2009, the FASB issued a new accounting standard, which amends existing revenue recognition accounting pronouncements and provides accounting principles and application guidance on whether multiple deliverables exist, how the arrangement should be separated and the consideration allocated. This standard eliminates the requirement to establish the fair value of undelivered products and services and instead provides for separate revenue recognition based upon management's estimate of the selling price for an undelivered item when there is no other means to determine the fair value of that undelivered item. Previously, accounting principles required that the fair value of the undelivered item be the price of the item either sold in a separate transaction between unrelated third parties or the price charged for each item when the item is sold separately by the vendor. Determining the fair value using these methods was difficult when the product was not individually sold because of its unique features. If the fair value of all of the elements in the arrangement was not determinable, then revenue was deferred until all of the items were delivered or fair value was determined. This new approach is effective prospectively for revenue arrangements entered into or materially modified in fiscal years beginning on or after June 15, 2010. We are currently evaluating the potential impact of this accounting standard on our condensed consolidated financial statements.

In June 2009, the FASB issued a new accounting standard which amends previously issued accounting guidance for the consolidation of a variable interest entity, or VIE, to require an enterprise to determine whether its variable interest or interests give it a controlling financial interest in a VIE. This amended consolidation guidance for VIEs also replaces the existing quantitative approach for identifying which enterprise should consolidate a VIE, which was based on which enterprise was exposed to a majority of the risks and rewards, with a qualitative approach, based on which enterprise has both (1) the power to direct the economically

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significant activities of the entity and (2) the obligation to absorb losses of the entity that could potentially be significant to the VIE or the right to receive benefits from the entity that could potentially be significant to the VIE. This new accounting standard has broad implications and may affect how we account for the consolidation of common structures, such as joint ventures, equity method investments, collaboration and other agreements, and purchase arrangements. Under this revised consolidation guidance, more entities may meet the definition of a VIE, and the determination about who should consolidate a VIE is required to be evaluated continuously. We adopted this standard effective January 1, 2010 and have determined that the adoption did not have an impact on our condensed consolidated financial statements.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK.

As part of our investment portfolio, we own financial instruments that are sensitive to market risks. The investment portfolio is used to preserve our capital until it is required to fund operations, including our research and development activities. Our marketable securities consist of U.S. government and municipal obligations, high-grade corporate notes and commercial paper. All of our investments in debt securities are classified as available-for-sale and are recorded at fair value. Our available-for-sale investments in debt securities are sensitive to changes in interest rates and changes in the credit ratings of the issuers. Interest rate changes would result in a change in the net fair value of these financial instruments due to the difference between the market interest rate and the market interest rate at the date of purchase of the financial instrument. If market interest rates were to increase immediately and uniformly by 50 basis points, or one-half of a percentage point, from levels at September 30, 2010, the net fair value of our interest-sensitive financial instruments would have resulted in a hypothetical decline of \$1.3 million. A downgrade in the credit rating of an issuer of a debt security or further deterioration of the credit markets could result in a decline in the fair value of the debt instruments. Our investment guidelines prohibit investment in auction rate securities and we do not believe we have any direct exposure to losses relating from mortgage-based securities or derivatives related thereto such as credit-default swaps. We have not recorded any impairment charges to our fixed income marketable securities during the nine months ended September 30, 2010.

ITEM 4. CONTROLS AND PROCEDURES.

Our management, with the participation of our chief executive officer and vice president of finance and treasurer, evaluated the effectiveness of our disclosure controls and procedures as of September 30, 2010. 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, 2010, our chief executive officer and vice president of finance and treasurer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

No change in our internal control over financial reporting (as defined in Rules 13a-15(d) and 15d-15(d) under the Exchange Act) occurred during the three months ended September 30, 2010 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

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PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS.

In June 2009, we joined with Max Planck in taking legal action against Whitehead, MIT and UMass. The complaint, initially filed in the Suffolk County Superior Court in Boston, Massachusetts and subsequently removed to the U.S. District Court for the District of Massachusetts, alleges, among other things, that the defendants have improperly prosecuted the so-called Tuschl I patent applications and wrongfully incorporated inventions covered by the so-called Tuschl II patent applications into the Tuschl I patent applications, thereby potentially damaging the value of inventions reflected in the Tuschl I and Tuschl II patent applications. In the field of RNAi therapeutics, we are the exclusive licensee of the Tuschl I patent applications from Max Planck, MIT and Whitehead, and of the Tuschl II patent applications from Max Planck.

The complaint seeks, among other things, a declaratory judgment regarding the prosecution of the Tuschl I patent family and unspecified monetary damages. In August 2009, Whitehead and UMass filed counterclaims against us and Max Planck, including for breach of contract. In January 2010, we and Max Planck filed an amended complaint expanding upon the allegations in the original complaint. We currently expect a jury trial to start in early 2011. In February 2010, we and Max Planck released MIT from any claims seeking monetary damages, and MIT has stipulated that it will be bound by any declaratory, injunctive, or equitable relief granted by the court.

In addition, in September 2009, the USPTO granted Max Planck's petition to revoke power of attorney in connection with the prosecution of the Tuschl I patent application. This action prevents the defendants from filing any papers with the USPTO in connection with further prosecution of the Tuschl I patent application without the agreement of Max Planck. Whitehead's petition to overturn this ruling was denied. Prosecution before the USPTO for both the Tuschl I and II pending patent applications was suspended pursuant to a standstill agreement. This agreement expired on September 15, 2010, and Max Planck, MIT, Whitehead and UMass agreed to file several continuation applications in the Tuschl I patent family to preserve their rights and maintain the status quo for these applications. Max Planck also filed a continuation application in the Tuschl II patent family.

Although we, along with Max Planck, are vigorously asserting our rights in this case, litigation is subject to inherent uncertainty and a court could ultimately rule against us and Max Planck. In addition, litigation is costly and may divert the attention of our management and other resources that would otherwise be engaged in running our business.

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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, will, plan, target, goal and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these words. Any or all of our forward-looking statements in this Quarterly Report on Form 10-Q and in any other public statements we make may turn out to be wrong. They can be affected by inaccurate assumptions we might make or by known or unknown risks and uncertainties. Many factors mentioned in the discussion below will be important in determining future results. Consequently, no forward-looking statement can be guaranteed. Actual future results may vary materially from those anticipated in forward-looking statements. We explicitly disclaim any obligation to update any forward-looking statements to reflect events or circumstances that arise after the date hereof. You are advised, however, to consult any further disclosure we make in our reports filed with the SEC.

Risks Related to Our Business

Risks Related to Being an Early Stage Company

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

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