Regulus Therapeutics Inc.
Form 10-Q
November 19, 2012
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UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 10-Q

(Mark One)

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

FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2012

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: 001-35670

Regulus Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	**26-4738379**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
3545 John Hopkins Ct., Suite 210, San Diego CA	**92121**
(Address of Principal Executive Offices)	**(Zip Code)**

858-202-6300

(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 x

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 x No ¨

Indicate by check mark whether 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 , smaller reporting company in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨	Accelerated filer ¨
Non-accelerated filer x (Do not check if a smaller reporting company)	Smaller reporting company ¨

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

As of November 16, 2012, the registrant had 35,829,029 shares of Common Stock ($0.001 par value) outstanding.

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REGULUS THERAPEUTICS INC.

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PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

Regulus Therapeutics Inc.

Condensed Balance Sheets

(In thousands, except share and par value amounts)

	September 30, 2012 (Unaudited)	December 31, 2011
Assets		
Current assets:		
Cash and cash equivalents	$ 17,426	$ 9,175
Short-term investments	13,467	28,969
Contract receivable	3,000	
Prepaids and other current assets	466	522
Total current assets	34,359	38,666
Property and equipment, net	3,144	3,110
Intangibles, net	1,124	980
Other assets	2,096	125
Total assets	$ 40,723	$ 42,881
Liabilities and stockholders deficit		
Current liabilities:		
Accounts payable	$ 649	$ 501
Accrued payroll	973	671
Accrued expenses	1,077	360
Income taxes payable		206
Current portion of other long-term obligations	115	377
Current portion of deferred revenue	10,593	10,735
Total current liabilities	13,407	12,850
Convertible notes payable	10,000	10,000
Convertible notes payable, at fair value	7,069	
Accrued interest on convertible notes payable	1,227	963
Other long-term obligations, less current portion	374	438
Deferred revenue, less current portion	16,602	16,987
Deferred rent	501	446
Total liabilities	49,180	41,684
Series A convertible preferred stock, $0.001 par value; 25,000,000 shares authorized, 24,900,000 shares issued and outstanding at September 30, 2012 (unaudited) and December 31, 2011; aggregate liquidation preference of $49,800 at September 30, 2012 (unaudited) and December 31, 2011	32,691	32,691
Series B convertible preferred stock, $0.001 par value; 2,500,000 shares authorized 2,499,999 shares issued and outstanding at September 30, 2012 (unaudited) and December 31, 2011; aggregate liquidation preference of $10,000 at September 30, 2012 (unaudited) and December 31, 2011	10,000	10,000
Stockholders deficit:		

Common stock, $0.001 par value; 38,600,000 shares authorized, 425,092 and 153,184 shares issued and outstanding at September 30, 2012 (unaudited) and December 31, 2011, respectively		
Additional paid-in capital	2,418	1,584
Accumulated other comprehensive loss	(23)	(67)
Accumulated deficit	(53,543)	(43,011)
Total stockholders deficit	(51,148)	(41,494)
Total liabilities and stockholders deficit	$ 40,723	$ 42,881

See accompanying notes.

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Regulus Therapeutics Inc.

Condensed Statements of Operations and Comprehensive Loss

(In thousands, except share and per share amounts)

	Three months ended September 30,		Nine months ended September 30,	
	2012	2011	2012	2011
	(Unaudited)			
Revenues:				
Revenue under strategic alliances	$ 2,809	$ 3,809	$ 9,462	$ 10,426
Total revenues	2,809	3,809	9,462	10,426
Operating expenses:				
Research and development	5,248	3,875	14,735	12,823
General and administrative	1,093	907	2,998	2,864
Total operating expenses	6,341	4,782	17,733	15,687
Loss from operations	(3,532)	(973)	(8,271)	(5,261)
Other income (expense):				
Interest income	20	28	74	96
Interest expense	(110)	(97)	(294)	(293)
Loss on extinguishment of debt	(1,738)		(1,738)	
Loss from valuation of convertible note payable	(331)		(331)	
Other income		1		2
Loss before income taxes	(5,691)	(1,041)	(10,560)	(5,456)
Income tax (benefit) expense	(6)	4	(28)	131
Net loss	$ (5,685)	$ (1,045)	$ (10,532)	$ (5,587)
Other comprehensive loss:				
Unrealized gain (loss) on short-term investments, net	10	(76)	44	(95)
Comprehensive loss	$ (5,675)	$ (1,121)	$ (10,488)	$ (5,682)
Net loss per share, basic and diluted	$ (15.98)	$ (11.68)	$ (41.03)	$ (76.97)
Shares used to compute basic and diluted net loss per share	355,735	89,438	256,682	72,588

See accompanying notes.

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Regulus Therapeutics Inc.

Condensed Statements of Cash Flows

(In thousands)

	Nine Months Ended September 30,	
	2012	2011
	(Unaudited)	
Operating activities		
Net loss	$ (10,532)	$ (5,587)
Adjustments to reconcile net loss to net cash (used in) operating activities		
Depreciation and amortization expense	741	656
Amortization of premium on investments, net	311	401
Gain on investments		(1)
Stock-based compensation	732	609
Loss on extinguishment of debt	1,738	
Loss from valuation of convertible note payable	331	
Change in operating assets and liabilities:		
Contract receivable	(3,000)	
Prepaids and other assets	56	(117)
Accounts payable	148	(609)
Accrued payroll	302	(318)
Accrued expenses	44	(258)
Accrued interest	263	242
Payables to related parties		81
Income taxes payable	(234)	130
Deferred revenue	(527)	(4,910)
Deferred rent	55	103
Net cash used in operating activities	(9,572)	(9,578)
Investing activities		
Purchases of short-term investments	(9,287)	(44,584)
Maturities and sales of short-term investments	24,550	44,140
Purchases of property and equipment	(724)	(237)
Acquisition of patents	(185)	(122)
Net cash provided by (used in) investing activities	14,354	(803)
Financing activities		
Principal payments on other long-term obligations	(326)	(307)
Proceeds from issuance of convertible notes payable	5,000	
Proceeds from exercise of common stock options	102	38
Costs paid in connection with initial public offering	(1,307)	
Net cash provided by (used in) financing activities	3,469	(269)
Net increase (decrease) in cash and cash equivalents	8,251	(10,650)
Cash and cash equivalents at beginning of period	9,175	21,268

Cash and cash equivalents at end of period	$ 17,426	$ 10,618
Supplemental disclosure of cash flow information		
Interest paid	$ 32	$ 51
Income taxes paid	$ 207	$
Supplemental disclosure of non-cash investing and financing activities		
Amounts accrued for property and equipment, net	$	$ (11)
Amounts accrued for patent expenditures, net	$ 10	$

See accompanying notes.

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Regulus Therapeutics Inc.

NOTES TO CONDENSED FINANCIAL STATEMENTS

(Unaudited)

1. The Business and Summary of Significant Accounting Policies

Description of Business

Regulus Therapeutics Inc. was originally formed as a Delaware limited liability company under the name Regulus Therapeutics LLC on September 6, 2007, and was converted to a Delaware corporation on January 2, 2009. As used in this report, unless the context suggests otherwise, the Company, our, us and we means Regulus Therapeutics Inc.

We are a biopharmaceutical company focused on discovering and developing first-in-class drugs that target *micro*RNAs to treat a broad range of diseases. We are using our *micro*RNA product platform to develop chemically modified, single-stranded oligonucleotides that we call anti-miRs. We use these anti-miRs to modulate *micro*RNAs and by doing so return diseased cells to their healthy state.

Basis of Presentation

We have prepared the accompanying unaudited condensed financial statements in accordance with accounting principles generally accepted in the United States of America for interim financial information and with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and disclosures required by generally accepted accounting principles for complete financial statements. In the opinion of our management, all adjustments (consisting of normal recurring adjustments) considered necessary for a fair presentation have been included. Operating results for the nine months ended September 30, 2012 are not necessarily indicative of the results that may be expected for the entire year. These financial statements should be read in conjunction with the audited financial statements and notes thereto for the year ended December 31, 2011 included in our final prospectus filed with the Securities and Exchange Commission on October 5, 2012 relating to our Registration Statement on Form S1/A (File No. 333-183384) for our initial public offering (IPO).

On September 7, 2012, our board of directors approved a one-for-two reverse stock split of our common stock. The accompanying financial statements and notes to the financial statements give retroactive effect to the reverse split for all periods presented.

Use of Estimates

Our unaudited condensed financial statements are prepared in accordance with accounting principles generally accepted in the United States (U.S. GAAP). The preparation of our financial statements requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our financial statements and accompanying notes. Our most significant estimates relate to revenue recognition and stock-based compensation. Although these estimates are based on our knowledge of current events and actions we may undertake in the future, actual results may ultimately differ from these estimates and assumptions.

Revenue Recognition

Our revenues generally consist of upfront payments for licenses or options to obtain licenses in the future, research and development funding and milestone payments under strategic alliance agreements, as well as funding received under government grants. We recognize revenues when all four of the following criteria are met: (1) persuasive evidence that an arrangement exists; (2) delivery of the products and/or services has occurred; (3) the selling price is fixed or determinable; and (4) collectibility is reasonably assured.

Milestones

In January 2011, we adopted new authoritative guidance on revenue recognition for milestone payments related to agreements under which we have continuing performance obligations. We recognize revenue from milestone payments when earned, provided that (i) the milestone event is substantive in that it can only be achieved based in whole or in part on either our performance or on the occurrence of a specific outcome resulting from our performance and its achievability was not reasonably assured at the inception of the agreement, (ii) we do not have ongoing performance obligations related to the achievement of the milestone and (iii) it would result in the receipt of additional payments. A milestone

payment is considered substantive if all of the following conditions are met: (i) the milestone payment is non-refundable; (ii) achievement of the milestone was not reasonably assured at the inception of the arrangement; (iii) substantive effort is involved to achieve the milestone; and (iv) the amount of the milestone payments appears reasonable in relation to the effort expended, the other milestones in the arrangement and the related risk associated with the achievement of the milestone. Any amounts received under the agreements in advance of performance, if deemed substantive, are recorded as deferred revenue and recognized as revenue as we complete our performance obligations. The adoption of this guidance did not materially change our previous method for recognizing milestone payments.

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Strategic Alliance Agreements entered into or materially modified after December 31, 2010

In January 2011, we adopted new authoritative guidance for multiple element arrangements. The guidance, which applies to multiple element agreements entered into or materially modified after December 31, 2010 amends the criteria for separating and allocating consideration in a multiple element agreement by modifying the fair value requirements for revenue recognition and eliminating the use of the residual method. Deliverables under the agreement will be accounted for as separate units of accounting provided that (i) a delivered item has value to the customer on a stand-alone basis; and (ii) if the agreement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the control of the vendor. The allocation of consideration amongst the deliverables under the agreement is derived using a best estimate of selling price if vendor-specific objective evidence and third-party evidence of fair value is not available. We did not enter into any significant multiple element agreements or materially modify any existing multiple element agreements during 2011. In June 2012, we materially modified our strategic alliance agreement with GlaxoSmithKline plc (GSK) and in July 2012, we materially modified our strategic alliance agreement with Sanofi. In August 2012, we entered into new collaboration and license agreements with both AstraZeneca AB (AstraZeneca) and Biogen Idec MA Inc. (Biogen Idec). For additional information see Note 7.

Deferred Revenue

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying balance sheets. Amounts not expected to be recognized within the next 12 months are classified as non-current deferred revenue.

Stock-Based Compensation

We account for stock-based compensation expense related to stock options granted to employees and members of our board of directors by estimating the fair value of each stock option on the date of grant using the Black-Scholes model. We recognize stock-based compensation expense using the accelerated multiple-option approach. Under the accelerated multiple-option approach (also known as the graded-vesting method), we recognize compensation expense over the requisite service period for each separately vesting tranche of the award as though the award was in substance multiple awards, resulting in accelerated expense recognition over the vesting period.

We account for stock options granted to non-employees, which primarily consist of members of our scientific advisory board, using the fair value approach. Stock options granted to non-employees are subject to periodic revaluation over their vesting terms.

The following table summarizes the weighted average assumptions we used in our Black-Scholes calculations:

	Three months ended September 30,		Nine months ended September 30,	
	2012	2011	2012	2011
Employee Stock Options:				
Risk-free interest rate	*	1.2%	1.1%	2.4%
Expected dividend yield	*	0.0%	0.0%	0.0%
Expected volatility	*	77.6%	71.0%	72.8%
Expected term (years)	*	6.1	6.1	6.1

* No stock options were granted during the three months ended September 30, 2012.

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The following table summarizes the allocation of our stock compensation expense (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2012	2011	2012	2011
Research and development	$ 278	$ 127	$ 461	$ 406
General and administrative	136	69	271	203
Total	$ 414	$ 196	$ 732	$ 609

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by dividing the net loss by the weighted-average number of common share equivalents outstanding for the period determined using the treasury-stock method. Dilutive common stock equivalents are comprised of convertible preferred stock and options outstanding under our stock option plan. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to our net loss position.

Potentially dilutive securities not included in the calculation of diluted net loss per share because to do so would be anti-dilutive are as follows (in common equivalent shares):

	Three months ended September 30,		Nine months ended September 30,	
	2012	2011	2012	2011
Convertible preferred stock outstanding	13,699,999	13,699,999	13,699,999	13,699,999
Common stock options	2,845,675	2,028,853	2,823,463	2,164,285
Total	16,545,674	15,728,852	16,523,462	15,864,284

In addition to the potentially dilutive securities noted above, as of September 30, 2012 we had $15.0 million principal amount of outstanding convertible notes payable that were potentially convertible into common stock upon the occurrence of various future stock financing events at prices that were not determinable until the occurrence of the future events. As such, we have excluded these convertible notes payable from the table above. Upon the completion of our IPO in October 2012, $10.0 million principal amount of the convertible notes (and related accrued interest) were converted into 2,703,269 shares of common stock. See Note 4 for information regarding the terms of the $5.0 million of convertible notes payable that became convertible into common stock upon, and remain outstanding after, our IPO.

Other Assets

Deferred IPO costs totaling $2.0 million are included in other assets at September 30, 2012. These costs represent legal, accounting and other direct costs related to our efforts to raise capital through a public sale of our common stock. We incurred no IPO costs prior to 2012. IPO costs were deferred until the completion of the IPO in October 2012, and such costs will be reclassified to additional paid-in capital as a reduction of the IPO proceeds.

Fair Value Option

Applicable accounting policies permit entities to choose, at specified election dates, to measure specified items at fair value if the decision about the election is: 1) applied instrument by instrument, 2) irrevocable, and 3) applied to an entire instrument. In addition, an entity may choose to elect the fair value option only at the date of an event (i.e., significant modifications of debt, as defined) that requires an eligible item to be measured at fair value at the time of the event but does not require fair value measurement at each reporting date after that.

In July 2012, we accounted for the amended and restated note issued to GSK in February 2010 as a debt extinguishment of the original note. We elected to measure the amended note under the fair value option. The difference between the carrying value of the original note and the fair value of the amended note was recorded as a loss on extinguishment of debt to non-operating earnings. Thereafter, any change to the fair value of the amended note will be recorded as gain (loss) from valuation of convertible notes payable to non-operating earnings.

Recent Accounting Pronouncements

In September 2011, a new accounting standard was issued that changed the disclosure requirements for the presentation of other comprehensive income (OCI) in the financial statements, including the elimination of the option to present OCI in our statements of stockholders deficit. We have elected to present OCI and its components for both interim and annual periods in a single statement which is our statement of operations and comprehensive loss. This standard was adopted as of January 1, 2012 and the retrospective application of this standard did not have a material impact on our financial statements.

2. Investments

We invest our excess cash in commercial paper and debt instruments of financial institutions, corporations, U.S. government-sponsored agencies, and the U.S. Treasury. As of September 30, 2012, our short-term investments had a weighted average maturity of less than one year.

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The following tables summarize our short-term investments (in thousands):

As of September 30, 2012	Maturity (in years)	Amortized cost	Unrealized Gains	Unrealized Losses	Estimated fair value
Certificates of deposit	1 or less	$ 1,640	$	$	$ 1,640
Commercial paper	1 or less	2,347			2,347
Corporate debt securities	1 or less	7,974	5	(1)	7,978
Debt securities of U.S. government-sponsored agencies	1 or less	1,501	1		1,502
Total		$ 13,462	$ 6	$ (1)	$ 13,467

As of December 31, 2011	Maturity (in years)	Amortized cost	Unrealized Gains	Unrealized Losses	Estimated fair value
Certificates of deposit	2 or less	$ 3,519	$	$	$ 3,519
Commercial paper	1 or less	4,599		(1)	4,598
Corporate debt securities	2 or less	13,139	5	(74)	13,070
Debt securities of U.S. government-sponsored agencies	1 or less	7,779	3		7,782
Total		$ 29,036	$ 8	$ (75)	$ 28,969

3. Fair Value Measurements

Applicable accounting guidance defines fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants as of the measurement date. Additionally, the guidance provides an established hierarchy for inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the most observable inputs be used when available. Observable inputs are inputs that market participants would use in valuing the asset or liability and are developed based on market data obtained from independent sources. Unobservable inputs are inputs that reflect our assumptions about the factors that market participants would use in valuing the asset or liability. There are three levels of inputs that may be used to measure fair value:

Level 1 includes financial instruments for which quoted market prices for identical instruments are available in active markets.

Level 2 includes financial instruments for which there are inputs other than quoted prices included within Level 1 that are observable for the instrument such as quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets with insufficient volume or infrequent transactions (less active markets) or model-driven valuations in which significant inputs are observable or can be derived principally from, or corroborated by, observable market data.

Level 3 includes financial instruments for which fair value is derived from valuation techniques in which one or more significant inputs are unobservable, including management s own assumptions.

The following table presents our fair value hierarchy for assets and liabilities measured at fair value on a recurring basis at September 30, 2012 and December 31, 2011 (in thousands):

	Fair value as of September 30, 2012			
	Total	Level 1	Level 2	Level 3
Cash equivalents	$ 15,625	$ 15,625	$	$
Certificates of deposit	1,640		1,640	
Commercial paper	2,347		2,347	
Corporate debt securities	7,978		7,978	
Debt securities of U.S. government-sponsored agencies	1,502		1,502	
Total assets	$ 29,092	$ 15,625	$ 13,467	$

	Fair Value Measurements Using Significant Unobservable Inputs (Level 3)
Balance at December 31, 2011	$
Transfer into Level 3 from election of fair value option	6,738
Change in estimated fair value of convertible notes payable	331
Balance at September 30, 2012	$ 7,069

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	Fair value as of September 30, 2012			
	Total	Level 1	Level 2	Level 3
Convertible notes payable	$ 7,069	$	$	$ 7,069
Total liabilities	$ 7,069	$	$	$ 7,069

	Fair value as of December 31, 2011			
	Total	Level 1	Level 2	Level 3
Cash equivalents	$ 8,078	$ 7,478	$ 600	$
Certificates of deposit	3,519		3,519	
Commercial paper	4,598		4,598	
Corporate debt securities	13,070		13,070	
Debt securities of U.S. government-sponsored agencies	7,782		7,782	
Total assets	$ 37,047	$ 7,478	$ 29,569	$

We obtain pricing information for our assets measured at fair value from quoted market prices or quotes from brokers/dealers. We generally determine the fair value of our investment securities using standard observable inputs, including reported trades, broker/dealer quotes, bids and/or offers.

On July 27, 2012, we amended and restated our $5.0 million convertible promissory note originally issued in February 2010 to GSK (2010 GSK note), which resulted in a debt extinguishment for accounting purposes. Concurrent with the debt extinguishment, we elected the fair value option for the 2010 GSK note. We used a third party valuation firm to value the 2010 GSK note at the extinguishment date and again at September 30, 2012. Based on the valuation, we recorded a $1.7 million loss on extinguishment of debt (the difference between the original $5.0 million carrying value and the fair value) on the Condensed Statements of Operations and Comprehensive Loss. In future periods, the fair value of the 2010 GSK note will be recorded on a quarterly basis with changes in fair value recorded in non-operating earnings. For the three and nine months ended September 30, 2012, we recorded a loss from valuation of convertible notes payable of $331,000 on the Condensed Statements of Operations and Comprehensive Loss.

The third-party valuation firm used an income approach in the form of a convertible bond valuation model to value the note. The convertible bond model considered the debt and option characteristics of the note. The key inputs to the model as of July 27, 2012 and September 30, 2012 were volatility (75%), risk-free rate (0.15%-0.71% and 0.15%-0.67%, respectively), and credit spread (11.0% and 10.5%, respectively). The absolute stock and strike price were not key inputs because upon an IPO, the conversion option is assumed to be set at-the-money. The estimated fair value of the note is based on the probability weighted average of an IPO and a Non-IPO scenario. The volatility inputs were based on historical and implied volatility of peer companies. Peer companies were consistent with those used previously in our 409A analyses. The risk-free rate inputs were based on the yield of US Treasury Strips as of each date. The credit spread inputs were based on a creditworthiness analysis of the Company and the guarantors of the February 2010 convertible promissory note, as applicable, and market rates for comparable straight debt instruments.

At September 30, 2012, the fair value of the note is classified as Convertible notes payable, at fair value on the Condensed Balance Sheet at $7.1 million ($5.0 million principal).

4. Convertible Notes Payable

In July 2012, we amended and restated the convertible promissory notes issued to GSK in April 2008 and February 2010 to provide, among other things, that (i) in the case of the $5.0 million note originally issued in April 2008, the principal amount plus interest under the note would, upon completion of our initial public offering in which we receive a minimum level of proceeds from new investors or that results in certain of our current stockholders together owning less than 50% of our voting securities, automatically convert into shares of our common stock at the initial public offering price and (ii) in the case of the $5.0 million note originally issued in February 2010, the principal amount plus accrued interest would, upon the completion of our initial public offering in which we receive a minimum level of proceeds from new investors or that results in certain of our current stockholders together owning less than 50% of our voting securities, become convertible, at the election of GSK, into shares of our common stock at the initial public offering price for a period of three years following such initial public offering. As of

September 30, 2012, both notes continued to accrue interest at the prime rate as published by The Wall Street Journal at the beginning of each calendar quarter, which for the quarter ended September 30, 2012, was 3.25%. In addition, as of September 30, 2012, both notes were set to mature in February 2013, if not earlier converted or repaid. The notes are guaranteed by Alnylam Pharmaceuticals, Inc. (Alnylam), and Isis Pharmaceuticals, Inc. (Isis), until the completion of our IPO. On October 10, 2012, upon the completion of our IPO, the $5.0 million note originally issued in April 2008 was converted into 1,447,037 shares of our common stock concurrently with the closing of the IPO at a conversion price of $4.00 per share. In addition, following the IPO, we cancelled the note issued to GSK in February 2010 and issued GSK a new note in the principal amount of $5.4 million, which accrues interest at 3.297% and has a maturity date of October 9, 2015. For additional information, see Note 8.

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We accounted for the amended and restated note issued to GSK in April 2008 as a debt modification. We accounted for the amended and restated 2010 GSK note as a debt extinguishment, and elected the fair value option as of the July 2012 amendment date. We recognized $1.7 million as loss on extinguishment of debt on the Condensed Statements of Operations and Comprehensive Loss and recorded the 2010 GSK note at $6.7 million on the Condensed Balance Sheets. At September 30, 2012, the fair value of the 2010 GSK note was recorded as $7.1 million on the Condensed Balance Sheets and we recognized $331,000 as Loss from valuation of convertible notes payable on the Condensed Statements of Operations and Comprehensive Loss for the three and nine months ended September 30, 2012.

In August 2012, we entered into a note purchase agreement with Biogen Idec, pursuant to which we issued Biogen Idec a convertible promissory note in the principal amount of $5.0 million. Unless earlier converted into our equity securities, all outstanding principal and accrued interest will become due on the maturity date, which will be the earlier of February 15, 2013 or the occurrence of a change in control. All outstanding principal and accrued interest under the convertible promissory note will convert into the same class of securities in our next qualified financing, which in the case of a private offering, is a financing in which new gross proceeds to us equal or exceed $10.0 million and in which case such conversion is at the election of Biogen Idec, and in the case of a public offering, is a firmly underwritten public offering pursuant to which all of our outstanding preferred stock is converted into common stock or pursuant to which we offer and sell at least $50.0 million of our common stock to the public and in which case such conversion is automatic. The price at which the convertible note will convert in such qualified financing will be the lowest price per share paid by other investors in such qualified financing, and if the conversion would cause Biogen Idec to own more than 5% of our outstanding capital stock, then the conversion may, at the election of Biogen Idec, be limited to a number of shares not to exceed 5% of our outstanding capital stock. The $5.0 million note and accrued interest thereunder of approximately $25,000 was converted into 1,256,232 shares of our common stock upon the closing of our initial public offering in October 2012 at a conversion price of $4.00 per share.

5. Stockholders Equity

Shares Reserved for Future Issuance

	September 30, 2012	December 31, 2011
Conversion of preferred stock	13,699,999	13,699,999
Common stock options outstanding	3,398,638	3,304,375
Common stock options available for future grant	731,781	228,638
Total common shares reserved for future issuance	17,830,418	17,233,012

6. Related-Party Transactions

The following table summarizes the amounts included in our operating expenses, which resulted from our activities with Isis (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2012	2011	2012	2011
Services performed by Isis	$	$ 141	$	$ 480
Out-of-pocket expenses paid by Isis				695
Sub-license fees paid to Isis				
Total	$	$ 141	$	$ 1,175

No amounts were due from or payable to any related parties as of September 30, 2012 or December 31, 2011.

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7. Strategic Alliances and Collaboration

The following table summarizes the amounts included in our revenues which resulted from our strategic alliances and collaboration (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2012	2011	2012	2011
GSK	$ 186	$ 1,309	$ 1,809	$ 2,926
Sanofi	2,500	2,500	7,530	7,500
AstraZeneca	94		94	
Biogen Idec	29		29	
Total	$ 2,809	$ 3,809	$ 9,462	$ 10,426

GSK

In June 2012, we and GSK amended our product development and commercialization agreement to extend the target selection period for the fourth collaboration target under the agreement. The modification made to the agreement was considered a material modification, which required the application of the new authoritative guidance adopted by us in January 2011 for multiple element arrangements. We determined that the elements within the strategic alliance should be treated as a single unit of accounting because the delivered elements, the opt-in licenses for *micro*RNA product candidates, did not have stand-alone value to GSK. As a result of the extension of the target selection period, we will recognize the remaining deferred revenue over approximately eight years, which we believe represents our new performance period under the amended agreement.

Immuno-Inflammatory Alliance

The immuno-inflammatory alliance also includes contractual milestones. If all the product candidates are successfully developed and commercialized through pre-agreed sales targets we could receive milestone payments up to $432.5 million, including up to $15.5 million for preclinical milestones, up to $87.0 million for clinical milestones, up to $150.0 million for regulatory milestones and up to $180.0 million for commercialization milestones. We are also entitled to receive tiered royalties as a percentage of annual sales which can increase up to the low end of the 10 to 20% range. In July 2011, we earned a milestone payment under the immuno-inflammatory alliance, and recognized revenue of $500,000.

We have evaluated the remaining contingent event-based payments under our strategic alliance agreement with GSK based on the new authoritative guidance for milestones and determined that the preclinical and clinical payments meet the definition of a substantive milestone because they are related to events (i) that can be achieved based in whole or in part on our performance or on the occurrence of a specific outcome resulting from our performance, (ii) for which there was substantive uncertainty at the date the agreement was entered into that the event would be achieved and (iii) that would result in additional payments being due to us. Accordingly, revenue for these achievements will be recognized in its entirety in the period when the milestone is achieved and collectibility is reasonably assured. Other contingent event-based payments under the strategic alliance agreement for which payment is contingent upon the results of GSK s performance will not be accounted for using the milestone method. Such payments will be recognized as revenue over the remaining estimated period of performance, if any, and when collectibility is reasonably assured. We can earn the following preclinical milestones: $500,000 upon the selection of a fourth *micro*RNA target and $5.0 million upon the selection of a development candidate for each of the selected three targets. We can also earn the following clinical milestones for each of the selected three targets: $4.0 million for the initiation of a Phase 1 clinical trial; $5.0 million for the initiation of a Phase 2 clinical trial; and $20.0 million if GSK chooses to opt-in to the program following the completion of a proof-of-concept trial.

HCV Alliance

The HCV alliance also includes contractual milestones. If the HCV program is successful, we could receive milestone payments up to $144.0 million, including up to $5.0 million for preclinical milestones, up to $29.0 million for clinical milestones, up to $50.0 million for regulatory milestones and up to $60.0 million for commercialization milestones. In addition, we will receive up to double-digit royalties on sales from any product that GSK successfully commercializes under this alliance.

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We have evaluated the remaining contingent event-based payments under our strategic alliance agreement with GSK based on the new authoritative guidance for milestones and determined that the preclinical and clinical payments meet the definition of a substantive milestone because they are related to events (1) that can be achieved based in whole or in part on our performance or on the occurrence of a specific outcome resulting from our performance, (2) for which there was substantive uncertainty at the date the agreement was entered into that the event would be achieved and (3) that would result in additional payments being due to us. Accordingly, revenue for these achievements will be recognized in its entirety in the period when the milestone is achieved and collectibility is reasonably assured. Other contingent event-based payments under the strategic alliance agreement for which payment is contingent upon the results of GSK s performance will not be accounted for using the milestone method. Such payments will be recognized as revenue over the remaining estimated period of performance, if any, and when collectibility is reasonably assured. We can earn a preclinical milestone of $5.0 million upon the selection of a development candidate. We can also earn the following clinical milestones: $4.0 million for initiation of a Phase 1 clinical trial; $5.0 million for the initiation of a Phase 2 clinical trial; and $20.0 million if GSK chooses to opt-in to the program following the completion of a proof-of-concept trial.

Sanofi

In July 2012, we amended and restated our collaboration and license agreement with Sanofi to expand the potential therapeutic applications of the *micro*RNA alliance targets to be developed under such agreement. The modification made to the agreement was considered a material modification, which required the application of the new authoritative guidance adopted by us in January 2011 for multiple element arrangements. We determined that the elements within the strategic alliance agreement with Sanofi should be treated as a single unit of accounting because the delivered elements did not have stand-alone value to Sanofi. The following three elements were delivered as part of the strategic alliance with Sanofi: (1) a license for up to four *micro*RNA targets; (2) an option to obtain a license for optional *micro*RNA compounds; and (3) an option to a research license under the Technology Alliance. As a result of our assessment, we will continue to recognize the remaining deferred revenue over five years, which we believe continues to represent our performance period under the amended agreement.

We have evaluated the remaining contingent event-based payments under our strategic alliance agreement with Sanofi based on the new authoritative guidance for milestones and determined that the preclinical payments meet the definition of a substantive milestone because they are related to events (i) that can be achieved based in whole or in part on our performance or on the occurrence of a specific outcome resulting from our performance, (ii) for which there was substantive uncertainty at the date the agreement was entered into that the event would be achieved and (iii) that would result in additional payments being due to us. Accordingly, revenue for these achievements will be recognized in its entirety in the period when the milestone is achieved and collectibility is reasonably assured. Other contingent event-based payments under the strategic alliance agreement for which payment is contingent upon the results of Sanofi s performance will not be accounted for using the milestone method. Such payments will be recognized as revenue over the remaining estimated period of performance, if any, and when collectibility is reasonably assured. We can earn the following preclinical milestones: $5.0 million upon the selection of each of the three remaining *micro*RNA targets; and $15.0 million upon the filing of an IND for each of the four *micro*RNA targets.

AstraZeneca

In August 2012, we entered into a collaboration and license agreement with AstraZeneca. Under the terms of the agreement, we have agreed to collaborate with AstraZeneca to identify, research and develop compounds targeting three *micro*RNA alliance targets primarily in the fields of cardiovascular diseases, metabolic diseases and oncology and granted to AstraZeneca an exclusive, worldwide license to thereafter develop, manufacture and commercialize lead compounds designated by AstraZeneca in the course of the collaboration activities against the alliance targets for all human therapeutic uses. Under the terms of the agreement we are required to use commercially reasonable efforts to perform all research, development and manufacturing activities described in the research plan, at our cost, until the acceptance of an IND or the end of the research term, which extends until the fourth anniversary of the date of the agreement, and may be extended only by mutual written agreement of us and AstraZeneca. Following the earlier to occur of the acceptance of an IND in a major market or the end of the research term, AstraZeneca will assume all costs, responsibilities and obligations for further development, manufacture and commercialization of alliance product candidates.

Under the terms of the agreement, we received an upfront payment of $3.0 million in October 2012. We considered the elements within the strategic alliance agreement as a single unit of accounting because the delivered element, the license, does not have stand-alone value. As a result, we are recognizing the upfront payment of $3.0 million to revenue on a straight-line basis over our estimated period of performance, which we have initially estimated to be four years based on the expected term of the research and development plan. If all three targets are successfully developed and commercialized through pre-agreed sales targets we could receive milestone payments up to $509.0 million, including up to $10.0 million for preclinical milestones, up to $129.0 million for clinical milestones, and up to $370.0 million for commercialization milestones. In addition, we are entitled to receive royalties based on a percentage of net sales which will range from the mid-single digits to the low end of the 10 to 20% range, depending upon the product and the volume of sales, which royalties may be reduced in certain, limited circumstances.

We have evaluated the contingent event-based payments under our strategic alliance agreement with AstraZeneca based on the new authoritative guidance for milestones and determined that the preclinical payments meet the definition of substantive milestones because they are related to events (i) that can be achieved based in whole or in part on our performance or on the occurrence of a specific outcome resulting from our performance, (ii) for which there was substantive uncertainty at the date the agreement was entered into that the event would be achieved and (iii) that would result in additional payments being due to us. Accordingly, revenue for these achievements will be recognized in its entirety in the period when the milestone is achieved and collectibility is reasonably assured. Other contingent event-based payments under the strategic alliance agreement for which payment is contingent upon the results of AstraZeneca s performance will not be accounted for using the milestone method. Such payments will be recognized as revenue over the remaining estimated period of performance, if any, and when collectibility is reasonably assured. We can earn the following preclinical milestones: $5.0 million for selection of a development candidate for *micro*RNA-33 (within a more limited time period) and $2.5 million for selection of a development candidate for each of the other two targets.

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Concurrently with the collaboration and license agreement, we entered into a common stock purchase agreement with AstraZeneca, pursuant to which we agreed to sell to AstraZeneca an aggregate of $25.0 million of our common stock concurrently with our initial public offering, at a price per share equal to the price at which we sell our common stock to the public in such initial public offering. In October 2012, in accordance with the common stock purchase agreement, we sold AstraZeneca 6,250,000 shares of our common stock at a price per share of $4.00 as further discussed in Note 8.

Biogen Idec

In August 2012, we entered into a collaboration and license agreement with Biogen Idec pursuant to which we and Biogen Idec have agreed to collaborate on *micro*RNA biomarkers for multiple sclerosis, or MS. Under the terms of the agreement, we granted Biogen Idec an exclusive, royalty free, worldwide license to our interest in the collaboration intellectual property for the purpose of commercializing non-*micro*RNA products for the treatment, diagnosis and prevention of MS and non-MS diseases and disorders. We also granted Biogen Idec an exclusive, royalty-free, worldwide license, with the right to sublicense, to our interest in the collaboration intellectual property (and a non-exclusive license to our background intellectual property) for the purpose of commercializing products for the diagnosis of MS. Biogen Idec granted us an exclusive, royalty-free, worldwide license, with the right to sublicense, to their interest in the collaboration intellectual property for the purpose of commercializing *micro*RNA products for the treatment of any disease, disorder or condition in humans. Pursuant to the agreement, we granted Biogen Idec a right of first negotiation on certain commercial transactions relating to *micro*RNA products which utilize intellectual property developed during the collaboration. Pursuant to the terms of the agreement, in August 2012 we received an upfront payment of $750,000. We are also eligible to receive research milestone payments of up to an aggregate of approximately $1.3 million. We considered the elements within the collaboration and license agreement as a single unit of accounting because the delivered element, the license, does not have stand-alone value. As a result, we are recognizing the upfront payment of $750,000 to revenue on a straight-line basis over our estimated period of performance, which we determined was approximately two years based on the expected term of the research and development plan.

We have evaluated the contingent event-based payments under our collaboration and license agreement with Biogen Idec based on the new authoritative guidance for milestones and determined that the research payments meet the definition of substantive milestones because they are related to events (i) that can be achieved based in whole or in part on our performance or on the occurrence of a specific outcome resulting from our performance, (ii) for which there was substantive uncertainty at the date the agreement was entered into that the event would be achieved and (iii) that would result in additional payments being due to us. Accordingly, revenue for these achievements will be recognized in its entirety in the period when the milestone is achieved and collectibility is reasonably assured. We can earn the following research milestones: $250,000 for identification of a *micro*RNA biomarker; $500,000 for validation of the *micro*RNA biomarker in a second independent sample set; and $500,000 upon the completion of a longitudinal study of patient samples on MS therapy.

Concurrently with the collaboration and license agreement, we entered into a note purchase agreement with Biogen Idec, pursuant to which we issued Biogen Idec a convertible promissory note in the principal amount of $5.0 million. The $5.0 million note and accrued interest thereunder of approximately $25,000 converted into 1,256,232 shares of our common stock upon the closing of our initial public offering in October 2012 at a conversion price of $4.00 per share.

8. Subsequent Events

Initial Public Offering and Other Financing Transactions

The unaudited pro forma balance sheet information below assumes the following transactions that were completed subsequent to September 30, 2012 had occurred on September 30, 2012:

On October 10, 2012, we completed our IPO whereby we sold 11,250,000 shares of common stock at $4.00 per share and received net proceeds of $40.7 million (after underwriting discounts and commissions and estimated offering costs not yet paid as of September 30, 2012);

On October 10, 2012, concurrent with the completion of our IPO, we sold 6,250,000 shares of common stock in a private placement to AstraZeneca at the initial public offering price of $4.00 per share and received net proceeds of $25.0 million;

On October 10, 2012, the automatic conversion of $5.0 million of outstanding principal plus accrued interest of $788,000 underlying a convertible note that we issued to GSK in April 2008 and amended and restated in July 2012 and the conversion of $5.0 million in outstanding principal plus accrued interest of $25,000 underlying a convertible note that we issued to Biogen Idec in August 2012, which together converted upon the completion of our IPO into an aggregate of 2,703,269 shares of our common stock. An aggregate of approximately $9,000 of interest was accrued from October 1, 2012 to October 10, 2012 which was included in the calculation of the shares issued but excluded from the pro forma adjustment to the accompanying balance sheet since such amounts were not yet accrued as of September 30, 2012;

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On October 10, 2012, the 27,399,999 outstanding shares of convertible preferred stock automatically converted into an aggregate of 13,699,999 shares of common stock upon the closing of our IPO;

On October 10, 2012, we filed an amended and restated certificate of incorporation to authorize 200,000,000 shares of common stock and 10,000,000 shares of undesignated preferred stock; and

On October 23, 2012, our underwriters partially exercised their option to purchase 1,480,982 additional shares of our common stock at $4.00 per share and we received net proceeds of $5.5 million (after underwriting discounts).

Pro forma net proceeds from our IPO and concurrent private placement were determined as follows (in thousands):

Gross proceeds (including over-allotment)	$ 75,924
Underwriting discounts and commissions	(3,366)
Estimated total offering costs	(2,600)
Offering costs paid as of September 30, 2012	1,307
Pro forma net proceeds	$ 71,265

The following table summarizes certain actual balance sheet data and pro forma balance sheet data to reflect the activities related to our IPO noted above, as of September 30, 2012 (in thousands):

	September 30, 2012	Pro forma September 30, 2012
Cash and cash equivalents	$ 17,426	$ 88,691
Other assets	2,096	125
Accounts payable and accrued expenses	1,726	1,062
Accrued interest	1,227	419
Convertible notes payable	10,000	
Convertible notes payable, at fair value	7,069	7,069
Convertible preferred stock	42,691	
Common stock		36
Additional paid-in capital	2,418	125,839
Total stockholders (deficit) equity	$ (51,148)	$ 72,309

Effective upon the closing of our IPO, 5,630,419 shares of common stock were reserved for future issuance under our 2012 equity incentive plan (2012 Plan), including 3,398,638 shares of common stock reserved for issuance upon the exercise of outstanding options issued under our 2009 equity incentive plan and 731,781 shares of common stock previously reserved for issuance under our 2009 equity incentive plan, in each case that were added to the shares reserved under the 2012 Plan upon its effectiveness.

Effective upon the closing of our IPO, 150,000 shares of common stock were reserved for future issuance under our 2012 employee stock purchase plan.

ITEM 2. MANAGEMENT S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

The interim unaudited condensed financial statements and this Management s Discussion and Analysis of Financial Condition and Results of Operations should be read in conjunction with the financial statements and notes thereto for the year ended December 31, 2011 and the related Management s Discussion and Analysis of Financial Condition and Results of Operations, both of which are contained in our final prospectus filed with the Securities and Exchange Commission on October 5, 2012 relating to our Registration Statement on Form S-1/A (File No. 333-183384) for our initial public offering.

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FORWARD-LOOKING STATEMENTS

This quarterly report on Form 10-Q may contain forward-looking statements within the meaning of the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth below under Part II, Item 1A, Risk Factors in this quarterly report on Form 10-Q. Except as required by law, we assume no obligation to update these forward-looking statements, whether as a result of new information, future events or otherwise. These statements, which represent our expectations or beliefs concerning various future events, may contain words such as may, will, expect, anticipate, intend, plan, believe, estimate or other words indicating futu Such statements may include, but are not limited to, statements concerning the following:

- the initiation, cost, timing, progress and results of our research and development activities, preclinical studies and future clinical trials;
- our ability to obtain and maintain regulatory approval of our future product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our future product candidates;
- our strategic alliance partners election to pursue development and commercialization;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our ability to obtain and maintain intellectual property protection for our future product candidates;
- the size and growth potential of the markets for our future product candidates, and our ability to serve those markets;
- our ability to successfully commercialize our future product candidates;
- the rate and degree of market acceptance of our future product candidates;
- our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;
- regulatory developments in the United States and foreign countries;
- the performance of our third-party suppliers and manufacturers;

the success of competing therapies that are or become available;

the loss of key scientific or management personnel;

our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;

our use of the proceeds from our recently completed initial public offering and private placement; and

the accuracy of our estimates regarding expenses, future revenues, capital requirements and need for additional financing.

OVERVIEW

We are a biopharmaceutical company focused on discovering and developing first-in-class drugs that target microRNAs to treat a broad range of diseases. We were formed in 2007 when Alnylam Pharmaceuticals, Inc., or Alnylam, and Isis Pharmaceuticals, Inc., or Isis, contributed significant intellectual property, know-how and financial and human capital to pursue the development of drugs targeting microRNAs pursuant to a license and collaboration agreement. microRNAs are recently discovered, naturally occurring ribonucleic acid, or RNA, molecules that play a critical role in regulating key biological pathways. Scientific research has shown the improper balance, or dysregulation, of microRNAs is directly linked to many diseases. We believe we have assembled the leading position in the microRNA field, including expertise in microRNA biology and oligonucleotide chemistry, a broad intellectual property estate, key opinion leaders and disciplined drug discovery and development processes. We refer to these assets as our microRNA product platform. We are using our microRNA product platform to develop chemically modified, single-stranded oligonucleotides that we call anti-miRs. We use these anti-miRs to modulate microRNAs and by doing so return diseased cells to their healthy state. We believe microRNAs may be transformative in the field of drug discovery and that anti-miRs may become a new and major class of drugs with broad therapeutic application much like small molecules, biologics and monoclonal antibodies. We are currently optimizing anti-miRs in five distinct programs, both independently and with our strategic alliance partners, AstraZeneca AB, or AstraZeneca, GlaxoSmithKline plc, or GSK, and Sanofi.

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Under these strategic alliances, we are eligible to receive up to approximately $1.7 billion in milestone payments upon successful commercialization of microRNA therapeutics for the eleven programs contemplated by our agreements. These payments include up to $106.5 million upon achievement of preclinical and investigational new drug application, or IND, milestones, up to $350.0 million upon achievement of clinical development milestones, up to $420.0 million upon achievement of regulatory milestones and up to $850.0 million upon achievement of commercialization milestones. We anticipate that we will nominate at least two clinical development candidates within the next 12 months and file at least two INDs with the U.S. Food and Drug Administration, or FDA, by 2014.

Recent developments

On October 10, 2012, we completed our IPO whereby we sold 11,250,000 shares of common stock at $4.00 per share and received net proceeds of $40.7 million (after underwriting discounts and commissions and estimated offering costs not yet paid as of September 30, 2012);

On October 10, 2012, concurrent with the completion of our IPO, we sold 6,250,000 shares of common stock in a private placement to AstraZeneca at the initial public offering price of $4.00 per share and received net proceeds of $25.0 million;

On October 10, 2012, the automatic conversion of $5.0 million of outstanding principal plus accrued interest of $788,000 underlying a convertible note that we issued to GSK in April 2008 and amended and restated in July 2012 and the conversion of $5.0 million in outstanding principal plus accrued interest of $25,000 underlying a convertible note that we issued to Biogen Idec in August 2012, which together converted upon the completion of our IPO into an aggregate of 2,703,269 shares of our common stock. An aggregate of approximately $9,000 of interest was accrued from October 1, 2012 to October 10, 2012 which was included in the calculation of the shares issued but excluded from the pro forma adjustment to the accompanying balance sheet since such amounts were not yet accrued as of September 30, 2012;

On October 10, 2012, the 27,399,999 outstanding shares of convertible preferred stock automatically converted into an aggregate of 13,699,999 shares of common stock upon the closing of our IPO;

On October 10, 2012, we filed an amended and restated certificate of incorporation to authorize 200,000,000 shares of common stock and 10,000,000 shares of undesignated preferred stock; and

On October 23, 2012, our underwriters partially exercised their option to purchase 1,480,982 additional shares of our common stock at $4.00 per share and we received net proceeds of $5.5 million (after underwriting discounts).

FINANCIAL OPERATIONS OVERVIEW

Revenues

Our revenues generally consist of upfront payments for licenses or options to obtain licenses in the future, research and development funding and milestone payments under strategic alliance agreements, as well as funding received under government grants.

In the future, we may generate revenue from a combination of license fees and other upfront payments, research and development payments, milestone payments, product sales and royalties in connection with strategic alliances. We expect that any revenue we generate will fluctuate from quarter-to-quarter as a result of the timing of our achievement of preclinical, clinical, regulatory and commercialization milestones, if at all, the timing and amount of payments relating to such milestones and the extent to which any of our products are approved and successfully commercialized by us or our strategic alliance partners. If our strategic alliance partners do not elect or otherwise agree to fund our development costs pursuant to our strategic alliance agreements, or we or our strategic alliance partners fail to develop product candidates in a timely manner or obtain regulatory approval for them, our ability to generate future revenues, and our results of operations and financial position would be adversely affected.

Research and development expenses

Research and development expenses consist of costs associated with our research activities, including our drug discovery efforts, the preclinical development of our therapeutic programs, and our *micro*RNA biomarker program. Our research and development expenses include:

employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;

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- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, or CROs, consultants and our scientific advisory board;

- license and sublicense fees; and

- facilities, depreciation and other allocated expenses, which include direct and allocated expenses for rent and maintenance of facilities, depreciation of leasehold improvements and equipment, and laboratory and other supplies.

We expense research and development costs as incurred. We account for nonrefundable advance payments for goods and services that will be used in future research and development activities as expenses when the service has been performed or when the goods have been received.

To date, we have conducted research on many different *micro*RNAs with the goal of understanding how they function and identifying those that might be targets for therapeutic modulation. At any given time we are working on multiple targets, primarily within our five therapeutic areas of focus. Our organization is structured to allow the rapid deployment and shifting of resources to focus on the best targets based on our ongoing research. As a result, in the early phase of our development, our research and development costs are not tied to any specific target. However, we are currently spending the vast majority of our research and development resources on our lead development programs.

Since our conversion to a corporation in January 2009, we have grown from 15 researchers to 34 and have spent a total of $61.2 million in research and development expenses through September 30, 2012.

We expect our research and development expenses to increase for the foreseeable future as we advance our research programs toward the clinic and initiate clinical trials. The process of conducting preclinical studies and clinical trials necessary to obtain regulatory approval is costly and time consuming. We or our strategic alliance partners may never succeed in achieving marketing approval for any of our product candidates. The probability of success for each product candidate may be affected by numerous factors, including preclinical data, clinical data, competition, manufacturing capability and commercial viability. Under our strategic alliance with GSK, we may be responsible for the development of product candidates through clinical proof-of-concept, depending on the time at which GSK may choose to exercise its option to obtain an exclusive license to develop, manufacture and commercialize product candidates on a program-by-program basis. Under our strategic alliance with Sanofi, we are responsible for the development of product candidates up to initiation of Phase 1 clinical trials, after which time Sanofi would be responsible for the costs of clinical development and commercialization and all related costs. Under our strategic alliance agreement with AstraZeneca, we are responsible for certain research and development activities with respect to each alliance target under a mutually agreed upon research and development plan until the earlier to occur of IND approval in a major market or the end of the research term under the agreement. We also have several independent programs for which we are responsible for all of the research and development costs, unless and until we partner any of these programs in the future.

Most of our product development programs are at an early stage, and successful development of future product candidates from these programs is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each future product candidate and are difficult to predict. We anticipate that we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to our ability to maintain or enter into new strategic alliances with respect to each program or potential product candidate, the scientific and clinical success of each future product candidate, as well as ongoing assessments as to each future product candidate s commercial potential. We will need to raise additional capital and may seek additional strategic alliances in the future in order to advance our various programs.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, legal, business development and support functions. Other general and administrative expenses include allocated facility-related costs not otherwise included in research and development expenses, travel expenses and professional fees for auditing, tax and legal services. We expect that general and administrative expenses will increase in the future as we expand our operating activities and incur additional costs associated with being a publicly-traded company. These increases will likely include legal fees, accounting fees, directors and officers liability insurance premiums and fees associated with investor relations.

Other income (expense), net

Other income (expense) includes interest income and expense, and on occasion income or expense of a non-recurring nature. We earn interest income from interest-bearing accounts and money market funds for cash and cash equivalents and marketable securities, such as interest-bearing

bonds, for our short-term investments. Interest expense represents the amounts payable to GSK and Biogen Idec under convertible notes and amounts paid under equipment and tenant improvement financing arrangements. In addition, we recognized a loss on the extinguishment of debt as a result of amending and restating our convertible note payable issued to GSK in February 2010. As a result of electing to value the note under the fair value option, we will recognize all changes to the fair value of the note as gain (loss) from valuation of convertible note payable.

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CRITICAL ACCOUNTING POLICIES AND SIGNIFICANT JUDGMENTS AND ESTIMATES

The preparation of our unaudited condensed financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities, disclosure of contingent assets and liabilities, and the revenues and expenses incurred during the reported periods. We base our estimates on historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We discussed accounting policies and assumptions that involve a higher degree of judgment and complexity within Note 1 to our financial statements in our Registration Statement on Form S-1/A (File No. 333-183384). Except as set forth in the paragraph below, there have been no material changes to our critical accounting policies and estimates from those disclosed in our Registration Statement on Form S-1/A (File No. 333-183384).

Fair Value Option

Applicable accounting policies permit entities to choose, at specified election dates, to measure specified items at fair value if the decision about the election is: 1) applied instrument by instrument, 2) irrevocable, and 3) applied to an entire instrument. In addition, an entity may choose to elect the fair value option only at the date of an event (i.e., significant modifications of debt, as defined) that requires an eligible item to be measured at fair value at the time of the event but does not require fair value measurement at each reporting date after that. In July 2012, we accounted for the amended and restated note issued to GSK in February 2010 as a debt extinguishment of the original note. We elected to measure the amended note under the fair value option. The difference between the carrying value of the original note and the fair value of the amended note was recorded as a loss on extinguishment of debt to non-operating earnings. Thereafter, any change to the fair value of the amended note will be recorded as gain (loss) from valuation of convertible notes payable to non-operating earnings.

RESULTS OF OPERATIONS

Comparison of the three months ended September 30, 2012 and 2011

The following table summarizes the results of our operations for the three months ended September 30, 2012 and 2011, together with the changes in those items in dollars (in thousands):

	Three months ended September 30,		
	2012	2011 (unaudited)	Increase/(Decrease)
Revenue under strategic alliances	$ 2,809	$ 3,809	$ (1,000)
Research and development expenses	5,248	3,875	1,373
General and administrative expenses	1,093	907	186
Loss on extinguishment of debt	(1,738)		1,738
Loss from valuation of convertible note payable	(331)		331

Revenue. We recognized revenue of $2.8 million in the three months ended September 30, 2012 and $3.8 million in the same period in 2011. Our revenue during these periods consisted primarily of amortization of upfront payments received from Sanofi and GSK which we amortize monthly on a straight-line basis over our period of performance. The total amortization attributable to payments from Sanofi was $2.5 million for each of the three months ended September 30, 2012 and 2011, and the total amortization attributable to payments from GSK was $186,000 for the three months ended September 30, 2012 and $1.3 million for the three months ended September 30, 2011. The decrease in the amount amortized for GSK for the three months ended September 30, 2012 compared to 2011 is the result of our June 2012 amendment to the collaboration agreement which extended our estimated period of performance and the resulting amortization period.

Research and development expenses. Research and development expenses were $5.2 million in the three months ended September 30, 2012 and $3.9 million for the same period in 2011. The increase of $1.4 million is related to a $124,000 increase in payroll expenses, a $508,000 increase in laboratory supplies, and a $660,000 increase in external services which was driven by additional hiring and efforts to advance our preclinical programs.

General and administrative expenses. General and administrative expenses were $1.1 million in the three months ended September 30, 2012 and $907,000 for the same period in 2011. The increase of $186,000 primarily represents legal services related to our transactions with AstraZeneca and Biogen Idec completed in August 2012.

Loss on extinguishment of debt. We recognized a $1.7 million loss on extinguishment of debt as a result of amending our $5.0 million 2010 GSK convertible promissory note in July 2012.

Loss from valuation of convertible note payable. We recognized a $331,000 loss as a result of the change in the fair value on the $5.0 million 2010 GSK convertible promissory note in July 2012.

Comparison of the nine months ended September 30, 2012 and 2011

The following table summarizes the results of our operations for the nine months ended September, 2012 and 2011, together with the changes in those items in dollars (in thousands):

	Nine months ended September 30,		
	2012	2011	Increase/(Decrease)
Revenue under strategic alliances and grants	$ 9,462	$ 10,426	$ (964)
Research and development expenses	14,735	12,823	1,912
General and administrative expenses	2,998	2,864	134
Loss on extinguishment of debt	(1,738)		1,738
Loss from valuation of convertible note payable	(331)		331

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Revenue. We recognized revenue of $9.5 million for the nine months ended September 30, 2012 and $10.4 million for the nine months ended September 30, 2011. Our revenue during these periods consisted primarily of amortization of upfront payments received from Sanofi and GSK which we amortize monthly on a straight-line basis over our period of performance. The total amortization attributable to payments from Sanofi was $7.5 million for each of the nine months ended September 30, 2012 and 2011, and the total amortization attributable to payments from GSK was $1.8 million for the nine months ended September 30, 2012 and $2.9 million for the nine months ended September 30, 2011. The decrease in the amount amortized for GSK is the result of our June 2012 amendment to the collaboration agreement which extended our estimated period of performance and the resulting amortization period.

Research and development expenses. Research and development expenses were $14.7 million for the nine months ended September 30, 2012 and $12.8 million for the nine months ended September 30, 2011. The increase of $1.9 million is related to a $311,000 increase in payroll expenses, a $842,000 increase in external services, and a $854,000 increase in laboratory supplies which was driven by additional hiring and efforts to advance our preclinical programs.

General and administrative expenses. General and administrative expenses were $3.0 million for the nine months ended September 30, 2012 and $2.9 million for the nine months ended September 30, 2011. The increase of $134,000 is primarily related to a $97,000 increase in accruals for our annual performance bonuses, and a $357,000 increase in consulting services and legal fees, the latter of which related to our transactions with AstraZeneca and Biogen Idec, offset by a $332,000 reduction in support services received from Isis.

Loss on extinguishment of debt. We recognized a $1.7 million loss on extinguishment of debt as a result of amending our $5.0 million 2010 GSK convertible promissory note in July 2012.

Loss from valuation of convertible note payable. We recognized a $331,000 loss as a result of the change in the fair value on the $5.0 million 2010 GSK convertible promissory note in July 2012

LIQUIDITY AND CAPITAL RESOURCES

From our inception in September 2007 through September 30, 2012, we have raised $116.6 million to fund our operations primarily through upfront payments, research funding and preclinical milestones from our strategic alliances, from government grants and from the sale of equity and convertible debt securities. As of September 30, 2012, we had received $61.6 million in upfront payments, research funding and preclinical milestones from our strategic alliances with GSK and Sanofi and government grants, and $55.0 million from the sale of equity and convertible debt securities.

As of September 30, 2012, we had $30.9 million in cash, cash equivalents and short-term investments. The following table shows a summary of our cash flows for the nine months ended September 30, 2012 and 2011:

	Nine months ended September 30,	
	2012	2011
	(unaudited)	
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$ (9,572)	$ (9,578)
Investing activities	14,354	(803)
Financing activities	3,469	(269)
Total	$ 8,251	$ (10,650)

Operating activities. Net cash used in operating activities were $9.6 million for each of the nine months ended September 30, 2012 and 2011. The primary drivers of the use of cash in operating activities for 2012 was the $3.0 million receivable outstanding from AstraZeneca at September 30, 2012, and amortization of deferred revenue relating to payments received under our strategic alliances of $9.4 million, offset by the addition of $8.8 million in deferred revenue related to R&D funding from Sanofi and our agreements with AstraZeneca and Biogen Idec entered into in August 2012. The primary driver of the use of cash in operating activities for 2011 was amortization of deferred revenue relating to payments received under our strategic alliances of $4.9 million. In addition, during the first quarter of 2011 we paid down our year-end accruals related to CROs and year-end management bonuses earned in 2010. The decrease in cash used from operating activities of $1.4 million between the nine months ended September 30, 2012 and 2011 was the result of lower payments made on our accounts payables and accrued

payroll, which includes prior year bonuses, during the first quarter of 2012.

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Investing activities. Net cash provided by or used in investing activities for periods presented primarily relate to the purchase, sale and maturity of investments used to fund the day-to-day needs of our business. In 2011, we reinvested substantially all our short-term securities upon maturity. In 2012, approximately $15.3 million of short-term maturities were used to fund our operations.

Financing activities. Net cash provided by financing activities was $3.4 million for the nine months ended September 30, 2012, compared to $269,000 used in financing activities for the same period in 2011. The primary driver of the cash provided by financing activities was the receipt of a $5.0 million convertible note from Biogen Idec in August 2012, offset by $1.3 million in payments related to our initial public offering.

Subsequent to September 30, 2012, we completed the following transactions:

On October 10, 2012, we completed our IPO of common stock pursuant to a Registration Statement that was declared effective on October 4, 2012. We sold 11,250,000 shares of our common stock, at a price of $4.00 per share. The underwriters exercised their over-allotment option on October 23, 2012, selling an additional 1,480,982 shares at $4.00 per share. As a result of the IPO, we raised a total of $44.9 million in net proceeds after deducting underwriting discounts and commissions of $3.4 million and offering expenses of $2.6 million. Costs directly associated with our IPO were capitalized and recorded as deferred IPO costs prior to the closing of the IPO. These costs have been recorded as a reduction of the proceeds received in arriving at the amount to be recorded in additional paid-in capital.

Upon the closing of the IPO, all shares of our convertible preferred stock automatically converted into 13,699,999 shares of our common stock. Also upon the closing of the IPO, $10.8 million of convertible notes (including accrued interest) converted into 2,703,269 shares of our common stock.

Concurrent with the closing of our IPO, we completed a $25.0 million private placement with AstraZeneca for $4.00 share and issued 6,250,000 shares of our common stock.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

The following is a summary of our long-term contractual obligations as of September 30, 2012 (in thousands):

		Payments due by period			
	Total	Less than 1 year	1 3 Years	3 5 Years	More than 5 years
Operating lease obligation relating to facility[1]	$ 3,092	$ 531	$ 1,256	$ 1,305	$
Principal under convertible notes payable, excluding accrued interest[2]	15,000	15,000			
Equipment financing obligation, including interest[3]	30	30			
Tenant improvement obligation, including interest[4]	535	113	225	197	
Total	$ 14,368	$ 900	$ 11,384	$ 1,642	$

(1) We lease 21,834 square feet for office and laboratory space in La Jolla, California under an operating lease that expires in June 2017.

(2) In April 2008, we issued a three-year convertible note to GSK in exchange for $5.0 million. In February 2010, we issued an additional three-year convertible note for $5.0 million. In January 2011, we and GSK amended the due date of the first convertible note payable to February 2013, which aligned the terms with those of the second note. Both convertible notes were amended and restated in July 2012. Until converted or cancelled, both convertible notes accrued interest at the prime rate as published by The Wall Street Journal at the beginning of each calendar quarter, which at the beginning of the third quarter of 2012, was 3.25%. We did not, and were under no obligation to, make periodic interest payments on either note, and as a result interest is not included in

the table above. Aggregate accrued interest as of September 30, 2012 was $1.2 million. Upon the completion of our IPO in October 2012, the principal and accrued interest under the first note automatically converted into shares of our common stock and the second note was amended and restated into a new convertible note with an adjusted face amount of $5.4 million. The new note matures on October 9, 2015 and bears interest at a rate of 3.297% per annum on the basis of a 360 day year.

(3) In September 2009, we entered into a $1.0 million credit facility to finance the purchase of lab equipment. The loan under this credit facility is secured by the assets financed under this obligation and is being repaid over 36 equal monthly installments. The interest rate is fixed at 5.9%.

(4) In conjunction with our lease, we were provided a tenant improvement allowance of $631,000, which was used to fund additional leasehold improvements. We are obligated to repay our landlord the tenant improvement allowance, plus interest at a fixed rate of 6.5%, on a monthly basis over the seven-year term of the lease.

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Off-Balance Sheet Arrangements

As of September 30, 2012, we did not have any off-balance sheet arrangements.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

Some of the securities that we invest in may have market risk in that a change in prevailing interest rates may cause the principal amount of the marketable securities to fluctuate. Financial instruments that potentially subject us to significant concentrations of credit risk consist primarily of cash, cash equivalents and short-term investments. We invest our excess cash primarily in commercial paper and debt instruments of financial institutions, corporations, U.S. government-sponsored agencies and the U.S. Treasury. The primary objectives of our investment activities are to ensure liquidity and to preserve principal while at the same time maximizing the income we receive from our marketable securities without significantly increasing risk. Additionally, we established guidelines regarding approved investments and maturities of investments, which are designed to maintain safety and liquidity.

Because of the short-term maturities of our cash equivalents and marketable securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our marketable securities. If a 10 percent change in interest rates were to have occurred on September 30, 2012, this change would not have had a material effect on the fair value of our investment portfolio as of that date.

ITEM 4. CONTROLS AND PROCEDURES

Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC s rules and forms, and that such information is accumulated and communicated to our management, including our chief executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily was required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, control may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As of September 30, 2012, we carried out an evaluation, under the supervision and with the participation of our management, including our chief executive officer and principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended. Based on this evaluation, our chief executive officer and principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of September 30, 2012.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

None.

ITEM 1A. RISK FACTORS

You should carefully consider the following risk factors, as well as the other information in this report, before deciding whether to purchase, hold or sell shares of our common stock. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You should consider all of the factors described when evaluating our business. We have marked with an asterisk (*) those risk factors that reflect changes from the risk factors included in our final prospectus filed with the

Securities and Exchange Commission on October 5, 2012 relating to our Registration Statement on Form S1/A (File No. 333-183384) for our initial public offering.

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RISKS RELATED TO OUR FINANCIAL CONDITION AND NEED FOR ADDITIONAL CAPITAL

We have a limited operating history, have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.*

We are a preclinical-stage, biopharmaceutical discovery and development company, formed in 2007, with a limited operating history. Since inception, our operations have been primarily limited to organizing and staffing our company, acquiring and in-licensing intellectual property rights, developing our *micro*RNA product platform, undertaking basic research around *micro*RNA targets and conducting preclinical studies for our initial programs. We have not yet identified product candidates for clinical development, initiated a clinical trial or obtained regulatory approval for any product candidates. Consequently, any predictions about our future success or viability, or any evaluation of our business and prospects, may not be accurate.

We have incurred losses in each year since our inception in September 2007. Our net losses were approximately $5.7 million and $1.0 million for the three months ended September 30, 2012 and 2011, and $10.5 million and $5.6 million for the nine months ended September 30, 2012 and 2011, respectively. As of September 30, 2012, we had an accumulated deficit of approximately $53.5 million.

We have devoted most of our financial resources to research and development, including our preclinical development activities. To date, we have financed our operations primarily through the sale of equity securities and convertible debt and from revenue received from our strategic alliance partners. We have entered into strategic alliances with Sanofi to develop our miR-21 programs for hepatocellular carcinoma, or HCC, and kidney fibrosis, with GSK, to develop our miR-122 program for hepatitis C virus infection, or HCV, and with AstraZeneca, to develop our miR-33 program for atherosclerosis. Under our agreement with GSK, GSK has an option to obtain exclusive worldwide licenses for the development, manufacture and commercialization of potential product candidates selected from our *micro*RNA product platform. If GSK exercises its option to obtain a license to develop, manufacture and commercialize such product candidates, GSK will assume responsibility for funding and conducting further clinical development and commercialization activities for such product candidates. However, if GSK does not exercise its option within the timeframes that we expect, or at all, or if Sanofi terminates its agreement with us, we will be responsible for funding further development of these product candidates and may not have the resources to do so unless we are able to enter into another strategic alliance for these product candidates. The size of our future net losses will depend, in part, on the rate of future expenditures and our ability to obtain funding through equity or debt financings, strategic alliances or grants. We have not initiated clinical development of any product candidate to date and it will be several years, if ever, before we have a product candidate ready for commercialization. Even if we or our strategic alliance partners successfully obtain regulatory approval to market a product candidate, our revenues will also depend upon the size of any markets in which our product candidates have received market approval, and our ability to achieve sufficient market acceptance and adequate market share for our products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. The net losses we incur may fluctuate significantly from quarter to quarter. We anticipate that our expenses will increase substantially if and as we: continue our research and preclinical development of our future product candidates, both independently and under our strategic alliance agreements; seek to identify additional *micro*RNA targets and product candidates; acquire or in-license other products and technologies; initiate clinical trials for our product candidates; seek marketing approvals for our product candidates that successfully complete clinical trials; ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; maintain, expand and protect our intellectual property portfolio; hire additional clinical, quality control and scientific personnel; and create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts.

We have never generated any revenue from product sales and may never be profitable.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic alliance partners, to successfully complete the development of, obtain the necessary regulatory approvals for and commercialize product candidates. We do not anticipate generating revenues from sales of products for the foreseeable future, if ever. Our ability to generate future revenues from product sales depends heavily on our success in:

- identifying and validating new *micro*RNAs as therapeutic targets;
- completing our research and preclinical development of future product candidates, including our miR-21, miR-122, miR-33 and miR-10b programs;

initiating and completing clinical trials for future product candidates;

seeking and obtaining marketing approvals for future product candidates that successfully complete clinical trials;

establishing and maintaining supply and manufacturing relationships with third parties;

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launching and commercializing future product candidates for which we obtain marketing approval, with an alliance partner or, if launched independently, successfully establishing a sales force, marketing and distribution infrastructure;

maintaining, protecting and expanding our intellectual property portfolio; and

attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of increased expenses and when we will be able to achieve or maintain profitability, if ever. In addition, our expenses could increase beyond expectations if we are required by the FDA or foreign regulatory agencies to perform studies and trials in addition to those that we currently anticipate.

Even if one or more of the future product candidates that we independently develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We may need to raise additional funding, which may not be available on acceptable terms, or at all.*

Developing pharmaceutical products, including conducting preclinical studies and clinical trials, is expensive. We expect our research and development expenses to substantially increase in connection with our ongoing activities, particularly as we advance our product candidates toward clinical programs. We will need to seek alternative financing or change our operational plans to continue as a going concern. We may need to raise additional funds to support our operations and such funding may not be available to us on acceptable terms, or at all.

We expect that our existing cash and cash equivalents, together with interest, will be sufficient to fund our current operations through at least the end of 2015. However, changing circumstances may cause us to consume capital more rapidly than we currently anticipate. For example, as we move our lead compounds through toxicology and other preclinical studies, also referred to as nonclinical studies, required to file an investigational new drug application, or IND, which may occur as early as 2014, we may have adverse results requiring that we find new product candidates, or our strategic alliance partners may not elect to pursue the development and commercialization of any of our *micro*RNA product candidates that are subject to their respective strategic alliance agreements with us. Any of these events may increase our development costs more than we expect. We may need to raise additional funds or otherwise obtain funding through strategic alliances if we choose to initiate clinical trials for new product candidates other than programs currently partnered. In any event, we will require additional capital to obtain regulatory approval for, and to commercialize, future product candidates. Raising funds in the current economic environment, when the capital markets have been affected by the global recession, may present additional challenges.

If we are required to secure additional financing, such additional fundraising efforts may divert our management from our day-to-day activities, which may adversely affect our ability to develop and commercialize future product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, if at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to:

significantly delay, scale back or discontinue the development or commercialization of any future product candidates;

seek strategic alliances for research and development programs at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or

relinquish or license on unfavorable terms, our rights to technologies or any future product candidates that we otherwise would seek to develop or commercialize ourselves.

If we are required to conduct additional fundraising activities and we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we will be prevented from pursuing development and commercialization efforts, which will have a material adverse effect on our business, operating results and prospects.

We may sell our equity or debt securities to fund our operations, which may result in dilution to our stockholders and impose restrictions on our business.*

In order to raise additional funds to support our operations, we may sell our equity or debt securities, which would result in dilution to all of our stockholders or impose restrictive covenants that adversely impact our business. The sale of additional equity or convertible securities would result in the issuance of additional shares of our capital stock and dilution to all of our stockholders. The incurrence of indebtedness would result in increased fixed payment obligations and could also result in certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. If we are unable to expand our operations or otherwise capitalize on our business opportunities, our business, financial condition and results of operations could be materially adversely affected and we may not be able to meet our debt service obligations.

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RISKS RELATED TO THE DISCOVERY AND DEVELOPMENT OF PRODUCT CANDIDATES

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

We have concentrated our therapeutic product research and development efforts on *micro*RNA technology, and our future success depends on the successful development of this technology and products based on our *micro*RNA product platform. Neither we nor any other company has received regulatory approval to market therapeutics targeting *micro*RNAs. The scientific discoveries that form the basis for our efforts to discover and develop product candidates are relatively new. The scientific evidence to support the feasibility of developing product candidates based on these discoveries is both preliminary and limited. If we do not successfully develop and commercialize product candidates based upon our technological approach, we may not become profitable and the value of our common stock may decline.

Further, our focus solely on *micro*RNA technology for developing drugs as opposed to multiple, more proven technologies for drug development increases the risks associated with the ownership of our common stock. If we are not successful in developing any product candidates using *micro*RNA technology, we may be required to change the scope and direction of our product development activities. In that case, we may not be able to identify and implement successfully an alternative product development strategy.

We may not be successful in our efforts to identify or discover potential product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize *micro*RNA therapeutics. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- our research methodology or that of our strategic alliance partners may be unsuccessful in identifying potential product candidates;
- potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval; or
- our strategic alliance partners may change their development profiles for potential product candidates or abandon a therapeutic area.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

All of our programs are still in preclinical development. Preclinical testing and clinical trials of our future product candidates may not be successful. If we are unable to successfully complete preclinical testing and clinical trials of our product candidates or experience significant delays in doing so, our business will be materially harmed.

We have invested a significant portion of our efforts and financial resources in the identification and preclinical development of product candidates that target *micro*RNAs. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our future product candidates. The success of our future product candidates will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;

obtaining and maintaining patent and trade secret protection for future product candidates;

establishing and maintaining manufacturing relationships with third parties or establishing our own manufacturing capability; and

successfully commercializing our products, if and when approved, whether alone or in collaboration with others.

If we do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to successfully complete the development of, or commercialize, our product candidates, which would materially harm our business.

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If clinical trials of our future product candidates fail to demonstrate safety and efficacy to the satisfaction of regulatory authorities or do not otherwise produce positive results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of our future product candidates.

Before obtaining marketing approval from regulatory authorities for the sale of future product candidates, we or our strategic alliance partners must then conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. The outcome of preclinical studies and early clinical trials may not be predictive of the success of later clinical trials, and interim results of a clinical trial do not necessarily predict final results. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for their products.

Events which may result in a delay or unsuccessful completion of clinical development include:

- delays in reaching an agreement with the FDA on final trial design;
- imposition of a clinical hold following an inspection of our clinical trial operations or trial sites by the FDA or other regulatory authorities;
- delays in reaching agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites;
- our inability to adhere to clinical trial requirements directly or with third parties such as CROs;
- delays in obtaining required institutional review board approval at each clinical trial site;
- delays in recruiting suitable patients to participate in a trial;
- delays in the testing, validation, manufacturing and delivery of the product candidates to the clinical sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- delays caused by patients dropping out of a trial due to product side effects or disease progression;
- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

If we or our strategic alliance partners are required to conduct additional clinical trials or other testing of any future product candidates beyond those that are currently contemplated, are unable to successfully complete clinical trials of any such product candidates or other testing, or if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we or our strategic alliance partners may:

- be delayed in obtaining marketing approval for our future product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or marketing approvals. We do not know whether any clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which would impair our ability to successfully commercialize our product candidates and may harm our business and results of operations. Any inability to successfully complete preclinical and clinical development, whether independently or with our strategic alliance partners, could result in additional costs to us or impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties.

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Any of our future product candidates may cause adverse effects or have other properties that could delay or prevent their regulatory approval or limit the scope of any approved label or market acceptance.

Adverse events, or AEs, caused by our future product candidates could cause us, other reviewing entities, clinical trial sites or regulatory authorities to interrupt, delay or halt clinical trials and could result in the denial of regulatory approval. Certain oligonucleotide therapeutics have shown injection site reactions and pro-inflammatory effects and may also lead to impairment of kidney or liver function. There is a risk that our future product candidates may induce similar adverse events.

If AEs are observed in any clinical trials of our future product candidates, including those that our strategic partners may develop under our alliance agreements, our or our partners ability to obtain regulatory approval for product candidates may be negatively impacted.

Further, if any of our future products, if and when approved for commercial sale, cause serious or unexpected side effects, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy;
- regulatory authorities may require the addition of labeling statements, such as warnings or contraindications;
- we may be required to change the way the product is administered or conduct additional clinical trials;
- we could be sued and held liable for harm caused to patients; or
- our reputation may suffer.

Any of these events could prevent us or our partners from achieving or maintaining market acceptance of the affected product and could substantially increase the costs of commercializing our future products and impair our ability to generate revenues from the commercialization of these products either by us or by our strategic alliance partners.

Even if we complete the necessary preclinical studies and clinical trials, we cannot predict whether or when we will obtain regulatory approval to commercialize a product candidate and we cannot, therefore, predict the timing of any revenue from a future product.

Neither we nor our strategic alliance partners can commercialize a product until the appropriate regulatory authorities, such as the FDA, have reviewed and approved the product candidate. The regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee recommends restrictions on approval or recommends non-approval. In addition, we or our strategic alliance partners may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process.

Even if we obtain regulatory approval for a product candidate, we will still face extensive regulatory requirements and our products may face future development and regulatory difficulties.

Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our future product candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. The holder of an approved new drug application, or NDA, is obligated to monitor and report AEs and any failure of a product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

In addition, drug product manufacturers and their facilities are subject to payment of user fees and continual review and periodic inspections by the FDA and other regulatory authorities for compliance with current good manufacturing practices, or cGMP, and adherence to commitments made in the NDA. If we or a regulatory agency discovers previously unknown problems with a product such as AEs of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions relative to that product or the manufacturing facility, including requiring recall or withdrawal of the product from the market or suspension of manufacturing.

If we or our partners fail to comply with applicable regulatory requirements following approval of any of our future product candidates, a regulatory agency may:

issue a warning letter asserting that we are in violation of the law;

seek an injunction or impose civil or criminal penalties or monetary fines;

suspend or withdraw regulatory approval;

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suspend any ongoing clinical trials;

refuse to approve a pending NDA or supplements to an NDA submitted by us;

seize product; or

refuse to allow us to enter into supply contracts, including government contracts.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response and could generate negative publicity. The occurrence of any event or penalty described above may inhibit our ability to commercialize our future products and generate revenues.

We may not be successful in obtaining or maintaining necessary rights to *micro*RNA targets, drug compounds and processes for our development pipeline through acquisitions and in-licenses.

Presently we have rights to the intellectual property, through licenses from third parties and under patents that we own, to modulate only a subset of the known *micro*RNA targets. Because our programs may involve a range of *micro*RNA targets, including targets that require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our future product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

For example, we sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution s rights in technology resulting from the collaboration. Regardless of such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

We may use our financial and human resources to pursue a particular research program or product candidate and fail to capitalize on programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and human resources, we intend to leverage our existing strategic alliance agreements and enter into new strategic alliance agreements for the development and commercialization of our programs and potential product candidates in indications with potentially large commercial markets such as HCC, fibrosis and HCV, while focusing our internal development resources and any internal sales and marketing organization that we may establish on research programs and future product candidates for selected markets, such as orphan diseases. As a result, we may forego or delay pursuit of opportunities with other programs or product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and future product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic alliance, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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Although we maintain workers compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES

We will depend upon our strategic alliances for the development and eventual commercialization of certain future *micro*RNA product candidates. If these strategic alliances are unsuccessful or are terminated, we may be unable to commercialize certain product candidates and we may be unable to generate revenues from our development programs.

We are likely to depend upon third party alliance partners for financial and scientific resources for the clinical development and commercialization of certain of our *micro*RNA product candidates. These strategic alliances will likely provide us with limited control over the course of development of a future *micro*RNA product candidate, especially once a candidate has reached the stage of clinical development. For example, in our alliance with GSK, GSK has the option to obtain an exclusive worldwide license to develop, manufacture and commercialize product candidates upon the achievement of relevant efficacy and safety endpoints in the first clinical trial designed to show efficacy, safety and tolerability with respect to each of four potential programs or earlier, at GSK s option. However, GSK is not under any obligation to exercise its option to progress any of our *micro*RNA development candidates. While each of AstraZeneca, GSK and Sanofi have development obligations with respect to programs that they may elect to pursue under their respective agreements, our ability to ultimately recognize revenue from these relationships will depend upon the ability and willingness of our alliance partners to successfully meet their respective responsibilities under our agreements with them. Our ability to recognize revenues from successful strategic alliances may be impaired by several factors including:

- an alliance partner may shift its priorities and resources away from our programs due to a change in business strategies, or a merger, acquisition, sale or downsizing of its company or business unit;
- an alliance partner may cease development in therapeutic areas which are the subject of our strategic alliances;
- an alliance partner may change the success criteria for a particular program or potential product candidate thereby delaying or ceasing development of such program or candidate;
- a significant delay in initiation of certain development activities by an alliance partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- an alliance partner could develop a product that competes, either directly or indirectly, with an alliance product;
- an alliance partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- an alliance partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- an alliance partner may exercise its rights under the agreement to terminate a strategic alliance;

- a dispute may arise between us and an alliance partner concerning the research, development or commercialization of a program or product candidate resulting in a delay in milestones, royalty payments or termination of a program and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and

- an alliance partner may use our proprietary information or intellectual property in such a way as to invite litigation from a third party or fail to maintain or prosecute intellectual property rights such that our rights in such property are jeopardized.

Specifically, with respect to termination rights, after expiration of an initial research term, Sanofi may terminate the entire alliance or any alliance target program for any or no reason upon 30 days written notice to us. The agreement with Sanofi may also be terminated by either party for material breach by the other party, including a failure to comply with such party s diligence obligations that remains uncured after 120 days. Similarly, GSK may terminate the entire alliance or any alliance target program for any or no reason upon 90 days written notice to us and the agreement may also be terminated by either party for material breach by the other party, including a failure to comply with such party s diligence obligations that remains uncured after a specified notice period. The agreement with AstraZeneca may be terminated by either party in the event of the other party s material breach which remains uncured after 40 business days following notice thereof (or 30 business days in the case of nonpayment). In addition, AstraZeneca may terminate the agreement in its entirety for any reason upon 60 business days written notice to us. Depending on the timing of any such termination, we may not be entitled to receive the option exercise fees or milestone payments, as these payments terminate with termination of the respective program or agreement.

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If any of our alliance partners do not elect to pursue the development and commercialization of our *micro*RNA development candidates or if they terminate the strategic alliance, then, depending on the event:

- in the case of Sanofi, under certain circumstances, we may owe Sanofi royalties with respect to product candidates covered by our agreement with Sanofi that we elect to continue to commercialize, depending upon the stage of development at which such product commercialization rights reverted back to us, or additional payments if we license such product candidates to third parties;
- the development of our product candidates subject to the AstraZeneca agreement, GSK agreement or Sanofi agreement, as applicable, may be terminated or significantly delayed;
- our cash expenditures could increase significantly if it is necessary for us to hire additional employees and allocate scarce resources to the development and commercialization of product candidates that were previously funded, or expected to be funded, by AstraZeneca, GSK or Sanofi, as applicable;
- we would bear all of the risks and costs related to the further development and commercialization of product candidates that were previously the subject of the AstraZeneca agreement, GSK agreement or Sanofi agreement, as applicable, including the reimbursement of third parties; and
- in order to fund further development and commercialization, we may need to seek out and establish alternative strategic alliances with third-party partners; this may not be possible, or we may not be able to do so on terms which are acceptable to us, in which case it may be necessary for us to limit the size or scope of one or more of our programs or increase our expenditures and seek additional funding by other means.

Any of these events would have a material adverse effect on our results of operations and financial condition.

We expect to rely on third parties to conduct some aspects of our compound formulation, research and preclinical testing, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such formulation, research or testing.

We do not expect to independently conduct all aspects of our drug discovery activities, compound formulation research or preclinical testing of product candidates. We currently rely and expect to continue to rely on third parties to conduct some aspects of our preclinical testing.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it would delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the study plan and protocols for the trial.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the necessary preclinical studies to enable us or our strategic alliance partners to select viable product candidates for IND submissions and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize such product candidates.

We intend to rely on third-party manufacturers to produce our preclinical supplies, and we intend to rely on third parties to produce clinical supplies of any product candidates that we advance into clinical trials and commercial supplies of any approved product candidates.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

the inability to meet any product specifications and quality requirements consistently;

a delay or inability to procure or expand sufficient manufacturing capacity;

manufacturing and product quality issues related to scale-up of manufacturing;

costs and validation of new equipment and facilities required for scale-up;

a failure to comply with cGMP and similar foreign standards;

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- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, and in some cases, single sources for raw materials, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell future product candidates in a timely fashion, in sufficient quantities or under acceptable terms;
- the lack of qualified backup suppliers for any raw materials that are currently purchased from a single source supplier;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- carrier disruptions or increased costs that are beyond our control; and
- the failure to deliver products under specified storage conditions and in a timely manner.

Any of these events could lead to clinical study delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

We expect to rely on limited sources of supply for the drug substance of future product candidates and any disruption in the chain of supply may cause a delay in developing and commercializing these product candidates.

We intend to establish manufacturing relationships with a limited number of suppliers to manufacture raw materials and the drug substance of any product candidate for which we are responsible for preclinical or clinical development. Each supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain. As part of any marketing approval, a manufacturer and its processes are required to be qualified by the FDA prior to commercialization. If supply from the approved vendor is interrupted, there could be a significant disruption in commercial supply. An alternative vendor would need to be qualified through an NDA supplement which could result in further delay. The FDA or other regulatory agencies outside of the United States may also require additional studies if a new supplier is relied upon for commercial production. Switching vendors may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

In addition, if our alliance partners elect to pursue the development and commercialization of certain programs, we will lose control over the manufacturing of the product candidate subject to the agreement. For example, if Sanofi elects to develop and commercialize a product candidate targeting miR-21 for HCC or kidney fibrosis under its strategic alliance with us, Sanofi will be responsible for the manufacture of the product candidates for clinical trials. Sanofi will be free to use a manufacturer of its own choosing or manufacture the product candidates in its own manufacturing facilities. In such a case, we will have no control over Sanofi s processes or supply chains to ensure the timely manufacture and supply of the product candidates. In addition, we will not be able to ensure that the product candidates will be manufactured under the correct conditions to permit the product candidates to be used in such clinical trials. Each of AstraZeneca and GSK will have similar obligations to manufacture product candidates which it takes into clinical trials under its strategic alliance with us and we will face similar risks as to those product candidates.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of our future product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to deliver the required commercial quantities of active pharmaceutical ingredients on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization.

As we scale-up manufacturing of future product candidates and conduct required stability testing, product, packaging, equipment and process-related issues may require refinement or resolution in order to proceed with any clinical trials and obtain regulatory approval for commercial marketing. We may identify significant impurities, which could result in increased scrutiny by the regulatory agencies, delays in clinical programs and regulatory approval, increases in our operating expenses, or failure to obtain or maintain approval for future product candidates or any approved products.

We expect to rely on third parties to conduct, supervise and monitor our clinical trials, and if those third parties perform in an unsatisfactory manner, it may harm our business.

If we or our strategic alliance partners commence clinical trials, we expect to rely on CROs and clinical trial sites to ensure the proper and timely conduct of our clinical trials. While we will have agreements governing their activities, we and our strategic alliance partners will have limited influence over their actual performance. We will control only certain aspects of our CROs activities. Nevertheless, we or our strategic alliance partners will be responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards and our reliance on the CROs does not relieve us of our regulatory responsibilities.

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We, our alliance partners and our CROs are required to comply with the FDA s cGCPs for conducting, recording and reporting the results of IND-enabling studies and clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces these cGCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable cGCPs, the clinical data generated in our future clinical trials may be deemed unreliable and the FDA may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with cGCPs. In addition, our future clinical trials will require a sufficiently large number of test subjects to evaluate the safety and effectiveness of a potential drug product. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

Our CROs will not be our employees, and we will not be able to control whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials, or other drug development activities which could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our future product candidates. As a result, our financial results and the commercial prospects for such products and any future product candidates that we develop would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

We also expect to rely on other third parties to store and distribute drug products for any clinical trials that we may conduct. Any performance failure on the part of our distributors could delay clinical development or marketing approval of our future product candidates or commercialization of our products, if approved, producing additional losses and depriving us of potential product revenue.

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

If we are unable to obtain or protect intellectual property rights related to our future products and product candidates, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our future products and product candidates. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own or in-license may fail to result in issued patents with claims that cover the products in the United States or in other foreign countries. There is no assurance that all of the potentially relevant prior art relating to our patents and patent applications has been found, which can invalidate a patent or prevent a patent from issuing based on a pending patent application. Even if patents do successfully issue, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims.

If the patent applications we hold or have in-licensed with respect to our programs or product candidates fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize, future products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. In particular, we are aware that Santaris Pharma A/S, or Santaris, has requested reexamination and filed oppositions to patents owned by Stanford University and licensed to us, in each case relating to miR-122, and has filed oppositions to a patent owned by us relating to miR-122 and to a patent owned by Isis relating to chemical modification of oligonucleotides. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we or our strategic alliance partners may develop. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by a third party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords, is limited. Once the patent life has expired for a product, we may be open to competition from generic medications.

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In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we expect all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA s disclosure policies may change in the future, if at all.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter partes reexamination proceedings before the U.S. Patent and Trademark Office, or U.S. PTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our strategic alliance partners are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our future product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our future product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our future product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our future product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our future product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.*

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We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. For example, under our exclusive license agreement for Max-Planck-Innovation GmbH s proprietary technology and know-how covering *micro*RNA sequences, we are required to use commercially reasonable diligence to develop and commercialize a product and to satisfy specified payment obligations. If we fail to comply with our obligations under our agreement with Max-Planck-Innovation GmbH or our other license agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we, or our strategic alliance partners, would not be able to market products covered by the license. In addition, our exclusive license agreements with our founding companies, Alnylam and Isis, provide us with rights to nucleotide technologies in the field of *micro*RNA therapeutics based on oligonucleotides that modulate up-regulated *micro*RNAs. Some of these technologies, such as intellectual property relating to the chemical modification of oligonucleotides, are relevant to our product candidate development programs. If our license agreements with Alnylam or Isis are terminated, or our business relationships with either of these companies or our other licensors are disrupted by events that may include the acquisition of either company, our access to critical intellectual property rights will be materially and adversely affected.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our future product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our future product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our alliance partners or licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

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RISKS RELATED TO COMMERCIALIZATION OF PRODUCT CANDIDATES

The commercial success of our miR-21, miR-122 and miR-33 programs, which are part of our strategic alliance agreements with Sanofi, GSK and AstraZeneca, respectively, will depend in large part on the development and marketing efforts of our alliance partners. If our alliance partners are unable to perform in accordance with the terms of our agreements, our potential to generate future revenue from these programs would be significantly reduced and our business would be materially and adversely harmed.

If any of Sanofi, GSK or AstraZeneca elects to pursue the development and commercialization of any of the *micro*RNA product candidates that are subject to their respective strategic alliance agreements with us, we will have limited influence and/or control over their approaches to development and commercialization. If Sanofi, GSK, AstraZeneca or any potential future strategic alliance partners do not perform in the manner that we expect or fail to fulfill their responsibilities in a timely manner, or at all, the clinical development, regulatory approval and commercialization efforts related to product candidates we have licensed to such strategic alliance partners could be delayed or terminated. If we terminate any of our strategic alliances or any program thereunder due to a material breach by Sanofi, GSK or AstraZeneca, we have the right to assume the responsibility at our own expense for the development of the applicable *micro*RNA product candidates. Assuming sole responsibility for further development will increase our expenditures, and may mean we will need to limit the size and scope of one or more of our programs, seek additional funding and/or choose to stop work altogether on one or more of the affected product candidates. This could result in a limited potential to generate future revenue from such *micro*RNA product candidates and our business could be materially and adversely affected. Further, under certain circumstances, we may owe Sanofi, GSK or AstraZeneca, as applicable, royalties on any product candidate that we may successfully commercialize.

We face significant competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive. We have competitors both in the United States and internationally, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. We are aware of several companies that are working specifically to develop *micro*RNA therapeutics including Groove Biopharma, Inc., miRagen Therapeutics, Inc., Mirna Therapeutics, Inc., and Santaris. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, drug products that are more effective or less costly than any product candidate that we may develop.

All of our programs are in a preclinical development stage and are targeted toward indications for which there are approved products on the market or product candidates in clinical development. We will face competition from other drugs currently approved or that will be approved in the future for the same therapeutic indications. Our ability to compete successfully will depend largely on our ability to leverage our experience in drug discovery and development to:

- discover and develop therapeutics that are superior to other products in the market;
- attract qualified scientific, product development and commercial personnel;
- obtain patent and/or other proprietary protection for our microRNA product platform and future product candidates;
- obtain required regulatory approvals; and
- successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new therapeutics.

The availability of our competitors products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize. We will not achieve our business plan if the acceptance of any of these products is inhibited by price competition or the reluctance of physicians to switch from existing drug products to our products, or if physicians switch to other new drug products or choose to reserve our future products for use in limited circumstances. The inability to compete with existing or subsequently introduced drug products would have a material adverse impact on our business, financial condition and prospects.

Established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our future product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate compelling advantages in efficacy, convenience, tolerability and safety in order to overcome price competition and to be commercially successful. Accordingly, our competitors may succeed in obtaining patent protection, receiving FDA approval or discovering, developing and commercializing product candidates before we do, which would have a material adverse impact on our business.

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The commercial success of our product candidates will depend upon the acceptance of these product candidates by the medical community, including physicians, patients and healthcare payors.

The degree of market acceptance of any product candidates will depend on a number of factors, including:

- demonstration of clinical safety and efficacy compared to other products;
- the relative convenience, ease of administration and acceptance by physicians, patients and healthcare payors;
- the prevalence and severity of any AEs;
- limitations or warnings contained in the FDA-approved label for such products;
- availability of alternative treatments;
- pricing and cost-effectiveness;
- the effectiveness of our or any collaborators sales and marketing strategies;
- our ability to obtain hospital formulary approval;
- our ability to obtain and maintain sufficient third party coverage or reimbursement; and
- the willingness of patients to pay out-of-pocket in the absence of third party coverage.

Unless other formulations are developed in the future, we expect our compounds to be formulated in an injectable form. Injectable medications may be disfavored by patients or their physicians in the event drugs which are easy to administer, such as oral medications, are available. If a product is approved, but does not achieve an adequate level of acceptance by physicians, patients and healthcare payors, we may not generate sufficient revenues from such product and we may not become or remain profitable.

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our future product candidates, we may be unable to generate any revenues.

We currently do not have an organization for the sales, marketing and distribution of pharmaceutical products and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. With respect to our current programs which are the subject of existing strategic alliances, such as miR-21 with Sanofi, miR-122 with GSK and miR-33 with AstraZeneca, we intend to rely completely on our alliance partner for sales and marketing. In addition, we intend to enter into strategic alliances with third parties to commercialize other future product candidates, including in markets outside of the United States or for other large markets that are beyond our resources. Although we intend to establish a sales organization if we are able to obtain approval to market any product candidates for niche markets in the United States, we will also consider the option to enter into strategic alliances for future product candidates in the United States if commercialization requirements exceed our available resources. This will reduce the revenue generated from the sales of these products.

Our current and future strategic alliance partners, if any, may not dedicate sufficient resources to the commercialization of our future product candidates or may otherwise fail in their commercialization due to factors beyond our control. If we are unable to establish effective alliances to enable the sale of our future product candidates to healthcare professionals and in geographical regions, including the United States, that will not be covered by our own marketing and sales force, or if our potential future strategic alliance partners do not successfully commercialize the product candidates, our ability to generate revenues from product sales will be adversely affected.

If we are unable to establish adequate sales, marketing and distribution capabilities, whether independently or with third parties, we may not be able to generate sufficient product revenue and may not become profitable. We will be competing with many companies that currently have extensive and well-funded marketing and sales operations. Without an internal team or the support of a third party to perform marketing and sales functions, we may be unable to compete successfully against these more established companies.

If we obtain approval to commercialize any approved products outside of the United States, a variety of risks associated with international operations could materially adversely affect our business.

Our strategic alliance agreements with Sanofi, GSK and AstraZeneca provide that our partners will be responsible for the commercialization of future product candidates, if any, from our miR-21, miR-122 and miR-33 programs, as applicable. If any other future product candidates that we may develop are approved for commercialization, we may also enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

different regulatory requirements for drug approvals in foreign countries;

reduced protection for intellectual property rights;

unexpected changes in tariffs, trade barriers and regulatory requirements;

economic weakness, including inflation, or political instability in particular foreign economies and markets;

compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;

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- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

Hospital formulary approval and reimbursement may not be available for our future product candidates, which could make it difficult for us to sell products profitably.

Obtaining formulary approval can be an expensive and time consuming process. We cannot be certain if and when we will obtain formulary approval to allow us to sell any products that we may develop and commercialize into our target markets. Failure to obtain timely formulary approval will limit our commercial success.

Furthermore, market acceptance and sales of any future product candidates that we develop will depend on reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third party payors, such as private health insurers, hospitals and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. We cannot be sure that reimbursement will be available for any future product candidates. Also, reimbursement amounts may reduce the demand for, or the price of, our future products. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize future product candidates that we develop.

There have been a number of legislative and regulatory proposals to change the healthcare system in the United States and in some foreign jurisdictions that could affect our ability to sell products profitably. These legislative and/or regulatory changes may negatively impact the reimbursement for drug products, following approval. The availability of numerous generic treatments may also substantially reduce the likelihood of reimbursement for our future products. The potential application of user fees to generic drug products may expedite the approval of additional generic drug treatments. We expect to experience pricing pressures in connection with the sale of any products that we develop, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. If we fail to successfully secure and maintain reimbursement coverage for our future products or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our future products and our business will be harmed.

RISKS RELATED TO OUR BUSINESS OPERATIONS AND INDUSTRY

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.*

We are highly dependent on principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are at will employees. Recruiting and retaining other qualified employees for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled executives in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical companies for individuals with similar skill sets. In addition, failure to succeed in preclinical studies and clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive or key employee might impede the progress of our research, development and commercialization objectives.

We will need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.*

As of September 30, 2012, we had 57 full-time employees. As our company matures, we expect to expand our employee base to increase our managerial, scientific and operational, commercial, financial and other resources and to hire more consultants and contractors. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize future product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

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Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs.

The use of our future product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by consumers, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. Certain oligonucleotide therapeutics have shown injection site reactions and pro-inflammatory effects and may also lead to impairment of kidney or liver function. There is a risk that our future product candidates may induce similar adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management s attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our future product candidates; and
- decreased demand for our future product candidates, if approved for commercial sale.

We do not currently have any product liability insurance coverage. We anticipate obtaining such insurance prior to the commencement of any clinical trials but any such insurance coverage that we obtain may not be sufficient to reimburse us for any expenses or losses we may suffer. Moreover, insurance coverage is becoming increasingly expensive and in the future we may not be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for future product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and, if judgments exceed our insurance coverage, could adversely affect our results of operations and

business.

Business interruptions could delay us in the process of developing our future products.

Our headquarters are located in San Diego County. We are vulnerable to natural disasters such as earthquakes and wild fires, as well as other events that could disrupt our operations. We do not carry insurance for earthquakes or other natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. Any losses or damages we incur could have a material adverse effect on our business operations.

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RISKS RELATED TO OUR COMMON STOCK

Our stock price may be volatile.*

Prior to our recently completed IPO, there was no public market for our common stock. The trading price of our common stock is likely to be volatile for the foreseeable future. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in preclinical testing or clinical trials;
- inability to obtain additional funding;
- any delay in filing an IND or NDA for any of our future product candidates and any adverse development or perceived adverse development with respect to the FDA s review of that IND or NDA;
- failure to maintain our existing strategic alliances or enter into new alliances;
- failure of our strategic alliance partners to elect to develop and commercialize product candidates under our alliance agreements or the termination of any programs under our alliance agreements;
- failure by us or our licensors and strategic alliance partners to prosecute, maintain or enforce our intellectual property rights;
- failure to successfully develop and commercialize our future product candidates;
- changes in laws or regulations applicable to future products;
- inability to obtain adequate product supply for our future product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;

the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;

announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic alliance partners or our competitors;

disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;

additions or departures of key scientific or management personnel;

significant lawsuits, including patent or stockholder litigation;

changes in the market valuations of similar companies;

sales of our common stock by us or our stockholders in the future; and

trading volume of our common stock.

In addition, companies trading in the stock market in general, and The NASDAQ Global Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

Our principal stockholders and management own a significant percentage of our stock and will be able to exert significant control over matters subject to stockholder approval.*

As of November 15, 2012, our executive officers, directors, 5% stockholders and their affiliates beneficially own approximately 72% of our outstanding voting stock. Therefore, these stockholders will have the ability to influence us through this ownership position. These stockholders may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

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We are an emerging growth company, and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.*

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have total annual gross revenue of $1.0 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1.0 billion in non-convertible debt during any three year period before that time, we would cease to be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a smaller reporting company which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies can also delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

The requirements of being a public company may strain our resources and divert management s attention.*

As a public company, we have incurred, and will continue to incur, significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, as well as rules subsequently implemented by the Securities and Exchange Commission, or SEC, and The NASDAQ Global Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as say on pay and proxy access. Recent legislation permits smaller emerging growth companies to implement many of these requirements over a longer period and up to five years from the pricing of our initial public offering. We intend to take advantage of this new legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

Sales of a substantial number of shares of our common stock in the public market by our existing stockholders could cause our stock price to fall.*

Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. We are unable to predict the effect that sales may have on the prevailing market price of our common stock.

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We, along with our directors, executive management team, holders of our convertible preferred stock, holders of our convertible notes and our strategic partners, including each of our founding companies, Alnylam and Isis, and each of AstraZeneca, GSK and Sanofi, have agreed that for a period of 365 days after the date of our final prospectus for our IPO dated October 4, 2012, subject to specified exceptions, we or they will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock. Substantially all of our other stockholders and option holders have agreed to similar obligations for a period of 180 days after the date of our final prospectus for our IPO dated October 4, 2012. Subject to certain limitations, approximately 26,848,047 shares will become eligible for sale upon expiration of the lock-up period. In addition, shares issued or issuable upon exercise of options vested as of the expiration of the lock-up period will be eligible for sale at that time. Sales of stock by these stockholders could have a material adverse effect on the trading price of our common stock.

Certain holders of our securities are entitled to rights with respect to the registration of their shares under the Securities Act of 1933, as amended, or the Securities Act, subject to the applicable lock-up arrangement described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by our affiliates as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.*

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2012 Equity Incentive Plan which became effective upon the closing of the IPO, or the 2012 plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2012 plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2012 plan each year. If our board of directors elects to increase the number of shares available for future grant by the maximum amount each year, our stockholders may experience additional dilution, which could cause our stock price to fall.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management s attention and resources, which could harm our business.

Our ability to use our net operating loss carryforwards and certain other tax attributes may be limited.

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an ownership change, generally defined as a greater than 50% change (by value) in its equity ownership over a three year period, the corporation s ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We believe that, with our initial public offering and other transactions that have occurred over the past three years, we may have triggered an ownership change limitation. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

We do not intend to pay dividends on our common stock so any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

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Provisions in our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders or remove our current management.

Some provisions of our charter documents and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders and may prevent attempts by our stockholders to replace or remove our current management. These provisions include:

- authorizing the issuance of blank check preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, we are subject to Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with an interested stockholder for a period of three years following the date on which the stockholder became an interested stockholder, unless such transactions are approved by our board of directors. This provision could have the effect of delaying or preventing a change in control, whether or not it is desired by or beneficial to our stockholders. Further, other provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us.

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Recent Sales of Unregistered Securities

From July 1, 2012 to September 30, 2012, we issued and sold an aggregate of 181,698 shares of our common stock to our employees and directors at a price of $0.38 per share for an aggregate of $69,045 pursuant to exercises of options granted under our 2009 equity incentive plan.

The sales and issuances of securities in the transactions described above were deemed to be exempt from registration under the Securities Act of 1933, as amended, in reliance upon Rule 701 promulgated under Section 3(b) of the Securities Act of 1933, as amended, as transactions pursuant to compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The recipients of securities in each transaction represented their intentions to acquire the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the securities issued in these transactions. All recipients had adequate access, through employment or other relationships, to information about us. All certificates representing the securities issued in these transactions included appropriate legends setting forth that the securities had not been offered or sold pursuant to a registration statement and describing the applicable restrictions on transfer of the securities. There were no underwriters employed in connection with any of the transactions set forth above.

Use of Proceeds

On October 4, 2012, we commenced our IPO pursuant to a registration statement on Form S-1 (File No. 333-183384) that was declared effective by the SEC on October 4, 2012 and that registered an aggregate of 12,937,500 shares of our common stock for sale to the public at a price of $4.00 per share and an aggregate offering price of $51,750,000. On October 10, 2012 and October 23, 2012, we sold 11,250,000 shares and 1,480,982 shares of our common stock, respectively, to the public at a price of $4.00 per share for an aggregate gross offering price of

$50,923,928. The offering has now terminated and consequently we may not sell under that registration statement the 206,518 remaining shares of common stock. Lazard Capital Markets, Cowen and Company and BMO Capital Markets acted as joint booking-running managers for the offering, and Needham & Company and Wedbush PacGrow Life Sciences served as co-managers for the offering.

The underwriting discounts and commissions in connection with the offering totaled approximately $3.4 million. We incurred additional costs of approximately $2.6 million in offering expenses, which when added to the underwriting discounts and commissions paid by us, amounts to total fees and costs of approximately $6.0 million. Thus, the net offering proceeds to us, after deducting underwriting discounts and commissions and offering costs, were approximately $44.9 million. No offering costs were paid directly or indirectly to any of our directors or officers (or their associates) or persons owning ten percent or more of any class of our equity securities or to any other affiliates.

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As of November 19, 2012, we have not used any of the net proceeds from the offering. We intend to use the net proceeds for preclinical and clinical development of our initial *micro*RNA development candidates, for the identification and validation of additional *micro*RNA targets, and for capital expenditures, working capital and other general corporate purposes, including costs and expenses associated with being a public company. We may also use a portion of the net proceeds to in-license, acquire or invest in complementary *micro*RNA businesses, technologies, products or assets. We cannot specify with certainty all of the particular uses for the net proceeds from our initial public offering. Accordingly, our management will have broad discretion in the application of the net proceeds.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURE

Not applicable.

ITEM 5. OTHER INFORMATION

None.

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ITEM 6. EXHIBITS

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation (incorporated by reference to Exhibit 3.1 to the Registrant s Current Report on Form 8-K, filed with the SEC on October 11, 2012)
3.2	Amended and Restated Bylaws (incorporated by reference to Exhibit 3.2 to the Registrant s Current Report on Form 8-K, filed with the SEC on October 11, 2012)
4.1	Form of Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.1 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.1+	Amended and Restated Collaboration and License Agreement between the Registrant and Sanofi, dated July 16, 2012 (incorporated by reference to Exhibit 10.31 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.2	Amendment Number Three to the Founding Investor Rights Agreement among the Registrant, Alnylam Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc., dated July 24, 2012 (incorporated by reference to Exhibit 10.36 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.3	Amended and Restated Convertible Promissory Note No. 1 made by the Registrant in favor of Glaxo Group Limited, dated July 27, 2012 (incorporated by reference to Exhibit 10.33 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.4	Amended and Restated Convertible Promissory Note No. 2 made by the Registrant in favor of Glaxo Group Limited, dated July 27, 2012 (incorporated by reference to Exhibit 10.34 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.5+	Collaboration and License Agreement between the Registrant and AstraZeneca AB, dated August 14, 2012 (incorporated by reference to Exhibit 10.37 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.6	Common Stock Purchase Agreement between the Registrant and AstraZeneca AB, dated August 14, 2012 (incorporated by reference to Exhibit 10.38 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.7+	Collaboration and License Agreement between the Registrant and Biogen Idec MA Inc., dated August 15, 2012 (incorporated by reference to Exhibit 10.39 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.8	Note Purchase Agreement between the Registrant and Biogen Idec MA Inc., dated August 15, 2012 (incorporated by reference to Exhibit 10.40 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.9	Convertible Promissory Note made by the Registrant in favor of Biogen Idec MA Inc., dated August 15, 2012 (incorporated by reference to Exhibit 10.41 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.10	Investor Rights Agreement, dated October 10, 2012, between AstraZeneca AB and the Registrant (incorporated by reference to Exhibit 10.1 to the Registrant s Current Report on Form 8-K, filed with the SEC on October 11, 2012)
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10.12	2012 Equity Incentive Plan and Form of Stock Option Agreement and Form of Stock Option Grant Notice thereunder (incorporated by reference to Exhibit 10.3 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)
10.13	Non-Employee Director Compensation Policy (incorporated by reference to Exhibit 10.4 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)

10.14	2012 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.5 of the Registrant s Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012)

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31.1*	Certification of Principal Executive Officer pursuant to Rules 13a-14 and 15d-14 promulgated pursuant to the Securities Exchange Act of 1934, as amended
31.2*	Certification of Principal Financial Officer pursuant to Rules 13a-14 and 15d-14 promulgated pursuant to the Securities Exchange Act of 1934, as amended
32.1*	Certification of Principal Executive Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2*	Certification of Principal Financial Officer pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101.INS	XBRL Instance Document
101.SCH	XBRL Taxonomy Extension Schema Document
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	XBRL Taxonomy Extension Label Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document

+ We have received confidential treatment of certain portions of this agreement, which have been omitted and filed separately with the SEC pursuant to Rule 406 under the Securities Act of 1933, as amended.
Indicates management contract or compensatory plan.

* These certifications are being furnished solely to accompany this quarterly report pursuant to 18 U.S.C. Section 1350, and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of the Registrant, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

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SIGNATURES

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

Regulus Therapeutics Inc.

Date: November 19, 2012

By: /s/ Kleanthis G. Xanthopoulos
Kleanthis G. Xanthopoulos, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

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