Regulus Therapeutics Inc.
Form 10-Q
November 14, 2013
Table of Contents

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, 2013

or

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
FOR THE TRANSITION PERIOD FROM _____ TO _____

Commission file number: 001-35670

Regulus Therapeutics Inc.

(Exact name of registrant as specified in its charter)

Delaware	**26-4738379**
(State or Other Jurisdiction of	**(I.R.S. Employer**
Incorporation or Organization)	**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 x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes 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 and smaller reporting company in Rule 12b-2 of the Exchange Act.

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

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 8, 2013, the registrant had 41,777,326 shares of Common Stock ($0.001 par value) outstanding.

Table of Contents

REGULUS THERAPEUTICS INC.

TABLE OF CONTENTS

PART I. FINANCIAL INFORMATION

Item 1.	Financial Statements	
	Condensed Balance Sheets as of September 30, 2013 (Unaudited) and December 31, 2012	3
	Condensed Statements of Operations and Comprehensive Loss for the three and nine months ended September 30, 2013 and 2012 (Unaudited)	4
	Condensed Statements of Cash Flows for the nine months ended September 30, 2013 and 2012 (Unaudited)	5
	Notes to Condensed Financial Statements (Unaudited)	6
Item 2.	Management s Discussion and Analysis of Financial Condition and Results of Operations	15
Item 3.	Quantitative and Qualitative Disclosures about Market Risk	21
Item 4.	Controls and Procedures	21

PART II. OTHER INFORMATION

Item 1.	Legal Proceedings	22
Item 1A.	Risk Factors	22
Item 2.	Unregistered Sales of Equity Securities and Use of Proceeds	41
Item 3.	Defaults Upon Senior Securities	42
Item 4.	Mine Safety Disclosures	42
Item 5.	Other Information	42
Item 6.	Exhibits	42

Table of Contents

PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

Regulus Therapeutics Inc.

CONDENSED BALANCE SHEETS

(In thousands, except share and per share data)

	September 30, 2013 (Unaudited)	December 31, 2012
Assets		
Current assets:		
Cash and cash equivalents	$ 33,490	$ 40,552
Short-term investments	90,413	57,548
Contracts and other receivables	95	
Prepaid and other current assets	1,288	829
Total current assets	125,286	98,929
Property and equipment, net	3,981	3,310
Intangibles, net	1,145	1,154
Other assets	178	125
Total assets	$ 130,590	$ 103,518
Liabilities and stockholders equity		
Current liabilities:		
Accounts payable	$ 1,140	$ 311
Accrued liabilities	1,705	658
Accrued compensation	1,228	1,348
Current portion of deferred revenue	9,454	10,451
Total current liabilities	13,527	12,768
Convertible notes payable, at fair value	13,921	10,134
Deferred revenue, less current portion	7,138	17,756
Other long-term liabilities	1,558	767
Total liabilities	36,144	41,425
Stockholders equity:		
Common stock, $0.001 par value; 200,000,000 shares authorized, 41,774,442 and 35,831,808 shares issued and outstanding at September 30, 2013 (unaudited) and December 31, 2012, respectively	42	36
Additional paid-in capital	171,608	122,528

Accumulated other comprehensive loss	(44)	(52)
Accumulated deficit	(77,160)	(60,419)
Total stockholders equity	94,446	62,093
Total liabilities and stockholders equity	$ 130,590	$ 103,518

See accompanying notes to these condensed financial statements.

Table of Contents

Regulus Therapeutics Inc.

CONDENSED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share data)

	Three months ended September 30,		Nine months ended September 30,	
	2013	2012	2013	2012
	(Unaudited)			
Revenues:				
Revenue under strategic alliances and collaborations	$ 6,118	$ 2,809	$ 14,115	$ 9,462
Total revenues	6,118	2,809	14,115	9,462
Operating expenses:				
Research and development	7,106	5,248	21,710	14,735
General and administrative	1,917	1,093	5,545	2,998
Total operating expenses	9,023	6,341	27,255	17,733
Loss from operations	(2,905)	(3,532)	(13,140)	(8,271)
Other income (expense):				
Interest and other income	72	20	207	74
Interest expense	(7)	(110)	(25)	(294)
Loss on extinguishment of debt		(1,738)		(1,738)
Gain (loss) from changes in valuation of convertible note payable	671	(331)	(3,787)	(331)
Loss before income taxes	(2,169)	(5,691)	(16,745)	(10,560)
Income tax benefit	(5)	(6)	(4)	(28)
Net loss	$ (2,164)	$ (5,685)	$ (16,741)	$ (10,532)
Other comprehensive loss:				
Unrealized gain on short-term investments, net	37	10	8	44
Comprehensive loss	$ (2,127)	$ (5,675)	$ (16,733)	$ (10,488)
Net loss per share:				
Basic	$ (0.05)	$ (15.98)	$ (0.45)	$ (41.03)
Diluted	$ (0.07)	$ (15.98)	$ (0.45)	$ (41.03)
Weighted average shares used to compute net loss per share:				
Basic	40,154,812	355,735	37,367,368	256,682

Diluted	41,555,660	355,735	37,367,368	256,682

See accompanying notes to these condensed financial statements.

Table of Contents

Regulus Therapeutics Inc.

Condensed Statements of Cash Flows

(In thousands)

	Nine months ended September 30,	
	2013	2012
	(Unaudited)	
Operating activities		
Net loss	$ (16,741)	$ (10,532)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization expense	996	741
Loss on extinguishment of debt		1,738
Loss from valuation of convertible note payable	3,787	331
Stock-based compensation	2,524	732
Amortization of premium on investments, net	1,018	311
Gain on investments	(6)	
Change in operating assets and liabilities:		
Contracts and other receivables	(95)	(3,000)
Prepaid and other assets	(512)	56
Accounts payable	829	148
Accrued liabilities	851	73
Accrued compensation	(120)	302
Deferred revenue	(11,615)	(527)
Deferred rent and other liabilities	68	55
Net cash used in operating activities	(19,016)	(9,572)
Investing activities		
Purchases of short-term investments	(50,390)	(9,287)
Maturities and sales of short-term investments	16,520	24,550
Purchases of property and equipment	(608)	(724)
Acquisition of intangibles	(46)	(185)
Net cash (used in) provided by investing activities	(34,524)	14,354
Financing activities		
Proceeds from issuance of common stock, net	46,562	102
Proceeds from issuance of convertible notes payable		5,000
Principal payments on other long-term obligations	(84)	(326)
Costs paid in connection with initial public offering		(1,307)
Net cash provided by financing activities	46,478	3,469

Net (decrease) increase in cash and cash equivalents	(7,062)	8,251
Cash and cash equivalents at beginning of period	40,552	9,175
Cash and cash equivalents at end of period	$ 33,490	$ 17,426
Supplemental disclosure of cash flow information		
Interest paid	$	$ 32
Income taxes paid	$ 1	$ 207
Supplemental disclosure of non-cash investing and financing activities		
Amounts accrued for property and equipment, net	$ 57	$
Amounts accrued for patent expenditures, net	$	$ 10

See accompanying notes to these financial statements.

Table of Contents

Regulus Therapeutics Inc.

NOTES TO CONDENSED FINANCIAL STATEMENTS

(Unaudited)

1. Basis of Presentation and Summary of Significant Accounting Policies

Basis of Presentation

The accompanying unaudited condensed financial statements have been prepared in accordance with U.S. generally accepted accounting principles (GAAP) for interim financial information and the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, they do not include all of the information and footnotes required by GAAP for complete financial statements. In management s opinion, the accompanying financial statements reflect all adjustments, consisting of normal recurring adjustments, considered necessary for a fair presentation of the results for the interim periods presented.

Interim financial results are not necessarily indicative of results anticipated for the full year. These unaudited condensed financial statements should be read in conjunction with the audited financial statements and footnotes included in the Annual Report on Form 10-K for the year ended December 31, 2012 for Regulus Therapeutics Inc. (we, us, our, or the Company), from which the balance sheet information herein for the year ended December 31, 2 was derived.

On September 7, 2012, our board of directors approved a one-for-two reverse stock split of our common stock. The accompanying condensed financial statements and notes to the condensed financial statements give retroactive effect to the reverse split for all periods presented. No further splits (or reverse splits) of our common stock have been contemplated as of September 30, 2013.

In October 2012, we completed an initial public offering and concurrent private placement of 18,980,982 shares of common stock at an offering price of $4.00 per share. In addition, principal and interest of $10.8 million from convertible notes outstanding were automatically converted upon the closing of the initial public offering into an aggregate of 2,703,269 shares of our common stock. We raised a total of $70.0 million in net proceeds from our initial public offering and concurrent private placement, after deducting underwriter discounts, commissions and other offering expenses.

In July 2013, we completed a public offering of 5,175,000 shares of common stock at an offering price of $9.50 per share. The shares were registered pursuant to a registration statement on Form S-1. We raised a total of $45.8 million in net proceeds, after deducting underwriting discounts, commissions and other offering expenses.

Use of Estimates

Our financial statements are prepared in accordance with 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. 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

As of September 30, 2013, we have ongoing strategic alliance agreements and collaborations with GlaxoSmithKline plc (GSK), Sanofi, AstraZeneca AB (AstraZeneca) and Biogen Idec MA Inc. (Biogen Idec). Our revenues generally consist of upfront payments for licenses or options to obtain licenses in the future, research and development funding and milestone payments. 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) collectability is reasonably assured.

For these multiple element arrangements, deliverables under our agreements are 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 units of accounting under our strategic alliance agreements and collaborations are derived using a best estimate of selling price if vendor specific objective evidence and third-party evidence of fair value is not available.

Milestones

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.

Table of Contents

Generally, the milestone events contained in our strategic alliance agreements and collaborations coincide with the progression of our product candidates from target selection, to clinical candidate selection, to clinical trial, to regulatory approval and then to commercialization. The process of successfully discovering a new development candidate, having it approved and ultimately sold for a profit is highly uncertain. As such, the milestone payments we may earn from our partners involve a significant degree of risk to achieve. Therefore, as a product candidate progresses through the stages of its life-cycle, the value of the product candidate generally increases.

Deferred Revenue

Amounts received prior to satisfying the above revenue recognition criteria are recorded as deferred revenue in the accompanying condensed 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 other than members of our board of directors, 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.

Fair Value Option

Applicable accounting guidance permits 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 July 2012, we amended and restated our $5.0 million convertible promissory note originally issued in February 2010 to GSK (2010 GSK Note), which was accounted for as a debt extinguishment of the original note. We elected to measure the 2010 GSK Note under the fair value option. Upon initial measurement, the difference between the carrying value of the original note and the fair value of the 2010 GSK Note was recorded as a loss on extinguishment of debt to non-operating earnings. Thereafter, any change to the fair value of the 2010 GSK Note is recorded as a gain (loss) from valuation of convertible note payable to non-operating earnings.

Recent Accounting Pronouncements

In February 2013, the FASB issued Accounting Standards Update No. 2013-02, *Comprehensive Income (Topic 220): Reporting of Amounts Reclassified Out of Accumulated Other Comprehensive Income* (ASU 2013-02). This update will require companies to present information about amounts reclassified out of accumulated other comprehensive income and their corresponding effect on net income in one place and reference the amounts to the related footnote disclosures. Current accounting standards present this information in different places throughout the financial statements. ASU 2013-02 was effective for us for the nine months ended September 30, 2013. The adoption of ASU 2013-02 had no impact on our financial condition, results of operations, or cash flows.

In July 2013, the FASB issued Accounting Standards Update No. 2013-11, *Presentation of an Unrecognized Tax Benefit When a Net Operating Loss Carryforward, a Similar Tax Loss, or a Tax Credit Carryforward Exists* (ASU 2013-11). This update provides explicit guidance on the financial statement presentation of an unrecognized tax benefit when a net operating loss carryforward, a similar tax loss, or a tax credit carryforward exists. This guidance is effective prospectively for fiscal years, and interim periods within those years, beginning after December 15, 2013, with an option for early adoption. We intend to adopt this guidance in 2014, and do not believe the adoption of this standard will have a material impact on our financial condition, results of operations or related financial statement disclosures.

2. 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 stock equivalents outstanding for the period determined using the treasury-stock method.

Table of Contents

Dilutive common stock equivalents are comprised of convertible preferred stock, options outstanding under our stock option plan and convertible notes payable. Applicable accounting guidance provides that a contract that is reported as an asset or liability for accounting purposes may require an adjustment to the numerator of the diluted earnings per share calculation for any changes in income or loss that would result if the contract had been reported as an equity instrument for accounting purposes during the period. Securities are assumed to be converted at the beginning of the period, and the resulting common shares are included in the denominator of the diluted earnings per share calculation for the entire period presented. Adding back the gain from the change in valuation of the convertible note payable for the three months ended September 30, 2013 to the numerator and adding the number of shares to be issued upon conversion of the convertible note payable into the denominator of the diluted earnings per share calculation resulted in an increase to the loss per share for the period. The convertible note payable was anti-dilutive for the nine months ended September 30, 2013.

The following table summarizes the adjustment to net loss for the diluted net loss per share calculation for the three months ended September 30, 2013 (in thousands):

Net loss	$ (2,164)
Less: gain from change in valuation of note payable	671
Net loss used to compute diluted net loss per share	$ (2,835)

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,	
	2013	2012	2013	2012
Convertible preferred stock outstanding		13,699,999		13,699,999
Common stock options	3,041,033	2,845,675	2,474,614	2,823,463
Convertible note payable			1,400,848	
Total	3,041,033	16,545,674	3,875,462	16,523,462

In October 2012, all convertible preferred stock converted into common stock in conjunction with our initial public offering. As of September 30, 2013 we had a convertible note payable outstanding with a principal balance of $5.4 million that was convertible into common shares at $4.00 per share, at the option of the note holder.

3. 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. For investments in debt securities with unrealized losses, we do not intend to sell these investments, nor is it more than likely that we will be required to do so, prior to the recovery of their amortized cost basis, which may be their maturity. As of September 30, 2013, our short-term investments had a weighted average maturity of less than two years.

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

	Maturity (in years)	Amortized cost	Unrealized Gains	Unrealized Losses	Estimated fair value
As of September 30, 2013					
Corporate debt securities	2 or less	$ 68,649	$ 18	$ (50)	$ 68,617
Commercial paper	1 or less	999			999
Certificates of deposit	2 or less	13,770			13,770
Debt securities of U.S. government-sponsored agencies	1 or less	7,025	2		7,027
Total		$ 90,443	$ 20	$ (50)	$ 90,413

Table of Contents

	Maturity (in years)	Amortized cost	Unrealized Gains	Unrealized Losses	Estimated fair value
As of December 31, 2012					
Corporate debt securities	2 or less	$ 44,898	$ 7	$ (49)	$ 44,856
Commercial paper	2 or less	6,492			6,492
Certificates of deposit	1 or less	6,200			6,200
Total		$ 57,590	$ 7	$ (49)	$ 57,548

4. Fair Value Measurements

We have certain financial assets and liabilities recorded at fair value which have been classified as Level 1, 2 or 3 within the fair value hierarchy as described in the accounting standards for 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. Market participants are buyers and sellers in the principal market that are (i) independent, (ii) knowledgeable, (iii) able to transact, and (iv) willing to transact. 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. The guidance prioritizes the inputs used in measuring the fair value into the following hierarchy:

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, 2013 and December 31, 2012 (in thousands):

	Fair value as of September 30, 2013			
	Total	Level 1	Level 2	Level 3
Assets:				

Cash equivalents	$ 33,377	$ 33,377	$	$
Corporate debt securities	68,617		68,617	
Commercial paper	999		999	
Certificates of deposit	13,770		13,770	
Debt securities of U.S. government-sponsored agencies	7,027		7,027	
	$ 123,790	$ 33,377	$ 90,413	$
Liabilities:				
Convertible notes payable	$ 13,921	$	$	$ 13,921

	Fair value as of December 31, 2012			
	Total	**Level 1**	**Level 2**	**Level 3**
Assets:				
Cash equivalents	$ 39,363	$ 39,363	$	$
Corporate debt securities	44,856		44,856	
Commercial paper	6,492		6,492	
Certificates of deposit	6,200		6,200	
	$ 96,911	$ 39,363	$ 57,548	$
Liabilities:				
Convertible notes payable	$ 10,134	$	$	$ 10,134

Table of Contents

Changes in the estimated fair value of convertible notes payable from December 31, 2012 through September 30, 2013 are as follows (in thousands):

	Fair Value Measurements Using Significant Unobservable Inputs (Level 3)
Balance at December 31, 2012	$ 10,134
Change in estimated fair value of convertible notes payable	3,787
Balance at September 30, 2013	$ 13,921

We obtain pricing information 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.

In July 2012, we amended and restated the 2010 GSK Note, which resulted in a debt extinguishment for accounting purposes. Concurrently with the debt extinguishment, we elected the fair value option for the 2010 GSK Note. The amended and restated 2010 GSK Note provided for a rollover of the 2010 GSK Note into a new promissory note effective as of the closing date of a qualifying initial public offering (Post-IPO GSK Note). We used a third party valuation firm to value the Post-IPO GSK Note at September 30, 2013 and recorded a gain from the change in valuation of the Post-IPO GSK Note of $0.7 million for the three months ended September 30, 2013 and a loss of $3.8 million for the nine months ended September 30, 2013 on the condensed statements of operations and comprehensive loss for the respective periods. The gain from the change in valuation of the Post-IPO GSK Note for the three months ended September 30, 2013 was principally driven by a reduction in our stock price to $9.43 as of September 30, 2013, compared to $9.81 as of June 30, 2013.

The third-party valuation firm used an income approach in the form of a convertible bond valuation model to value the Post-IPO GSK Note. The convertible bond model considered the debt and option characteristics of the Post-IPO GSK Note. The key inputs to the model as of September 30, 2013 were stock price, volatility (65%), risk-free rate (0.32%), and credit spread (8.5%). The volatility inputs were based on historical and implied volatility of peer companies. Peer companies were materially consistent with those used previously in our 409A analyses and in previous valuations of this instrument. The risk-free rate inputs were based on the yield of U.S. Treasury Strips as of each date. The credit spread inputs were based on a creditworthiness analysis of the Company and market rates for comparable straight debt instruments.

5. Convertible Notes Payable

2012 Amendment of the 2010 GSK Note

In July 2012, we amended and restated our 2010 GSK Note. In October 2012, in conjunction with our initial public offering, we issued the Post-IPO GSK Note in the principal amount of $5.4 million, which was equivalent to the original principal amount of $5.0 million plus accrued but unpaid interest of approximately $0.4 million. The amended and restated 2010 GSK Note was then simultaneously cancelled and our obligations thereunder terminated. The

Post-IPO GSK Note has a maturity date of October 9, 2015. At GSK s option, the Post-IPO GSK Note may be converted into shares of our common stock at any time prior to the maturity at a conversion price per share equal to the initial public offering price of $4.00, subject to complying with certain threshold ownership percentage limitations set forth in the Post-IPO GSK Note. At September 30, 2013, the fair value of the Post-IPO GSK Note is $13.9 million and is classified as Convertible note payable, at fair value on the condensed balance sheet.

6. Stockholders Equity

Shares Reserved for Future Issuance

The following shares of common stock are reserved for future issuance at September 30, 2013:

Table of Contents

	September 30, 2013	December 31, 2012
Common stock options outstanding	4,160,215	4,661,549
Common stock options available for future grant	2,161,410	946,403
Employee Stock Purchase Plan	460,283	150,000
Convertible note payable	1,400,848	1,366,787
Total common shares reserved for future issuance	8,182,756	7,124,739

The following table summarizes our stock option activity under all stock option plans for the nine months ended September 30, 2013 (in thousands):

	Number of options	Weighted average exercise price
Options outstanding at December 31, 2012	4,720	$ 2.11
Granted	361	$ 7.91
Exercised	(720)	$ 0.80
Canceled/forfeited/expired	(201)	$ 3.44
Options outstanding at September 30, 2013	4,160	$ 2.78

Stock-Based Compensation

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,	
	2013	2012	2013	2012
Employee Stock Options:				
Risk-free interest rate	1.7%	*	1.4%	1.1%
Expected dividend yield	0.0%	*	0.0%	0.0%
Expected volatility	72.7%	*	67.8%	71.0%
Expected term (years)	6.1	*	6.1	6.1

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

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

	Three months ended September 30,		Nine months ended September 30,	
	2013	2012	2013	2012

Research and development	$ 594	$ 278	$ 1,664	$ 461
General and administrative	384	136	860	271
Total	$ 978	$ 414	$ 2,524	$ 732

7. Strategic Alliances and Collaborations

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

	Three months ended September 30,		Nine months ended September 30,	
	2013	2012	2013	2012
Sanofi	$ 5,422	$ 2,500	$ 10,828	$ 7,530
GSK	144	186	1,634	1,809
AstraZeneca	465	94	1,394	94
Biogen Idec	87	29	259	29
Total	$ 6,118	$ 2,809	$ 14,115	$ 9,462

Table of Contents

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 elements were delivered as part of the strategic alliance with Sanofi: (1) a license for up to four *micro*RNA targets; and (2) a research license under our technology alliance.

In June 2013, the original research term expired, upon which we and Sanofi entered into an option agreement pursuant to which we granted Sanofi an exclusive right to negotiate the co-development and commercialization of certain of our unencumbered *micro*RNA programs and we were granted the exclusive right to negotiate with Sanofi for co-development and commercialization of certain miR-21 anti-miRs in oncology and Alport s Syndrome. These options expire in December 2013, subject to a 30-day extension in certain circumstances. In July 2013, we received an upfront payment of $2.5 million, of which $1.25 million is creditable against future amounts payable by Sanofi to us under any future co-development and commercialization agreement we enter pursuant to the option agreement. The non-creditable portion of this payment, $1.25 million, will be recognized as revenue over the option period from the effective date of the option agreement in June 2013 until the expiration of the option period in December 2013. Revenue associated with the creditable portion of this option payment will be deferred until the option period expires, or is re-evaluated in connection with a creditable transaction. In addition, we agreed to continue specified research on the miR-21 programs during the option period. As a result of the expiration of the original research term and subsequent option agreement, we re-evaluated our estimated period of performance and are now amortizing the remaining deferred revenue of $10.1 million associated with the initial upfront payment of $25.0 million ratably from June 2013 until the expiration of the option period in December 2013.

We have evaluated the remaining contingent event-based payments under our strategic alliance agreement with Sanofi 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 collectability 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 collectability is reasonably assured. As of the expiration of the research term in June 2013, Sanofi no longer has rights to select additional *micro*RNA targets. As such, we can earn a preclinical milestone of $15.0 million upon the filing of an Investigational New Drug application (IND) for the selected *micro*RNA target. We can also receive milestone payments of up to $33.0 million for clinical milestones and up to $165.0 million for regulatory and commercial milestones. In addition, we are entitled to receive royalties based on a percentage of net sales which will range from 8 to 12%, depending upon the volume of sales.

GSK

In April 2008, we entered into a strategic alliance with GSK to discover, develop and commercialize novel microRNA-targeted therapeutics to treat inflammatory diseases (the immuno-inflammatory alliance). In February 2010, we and GSK expanded the strategic alliance to include hepatitis C virus infection (HCV) to discover, develop

and commercialize microRNA therapeutics targeting miR-122 for the treatment of HCV (the HCV alliance). In June 2012, we amended our product development and commercialization agreement with GSK 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 extended the amortization period for the remaining deferred revenue to approximately eight years, which represented our new estimated performance period under the amended agreement. As of September 30, 2013, deferred revenue associated with the product development and commercialization agreement was $3.7 million.

In June 2013, the product development and commercialization agreement with GSK was amended to state that RG-101, and other formulations thereof, will be developed by us independently of our alliance with GSK for the treatment of chronic HCV infection. This amendment removed any further milestone or royalty obligations owed by GSK to us as it relates to RG-101. Concurrent with the amendment, we accelerated the remaining unamortized $1.1 million in deferred revenue associated with the upfront payment from the February 2010 amendment that expanded our agreement with GSK to include potential *micro*RNA therapeutics for the treatment of HCV, which represents that our estimated performance period under the amended agreement is complete.

Table of Contents

HCV Alliance

Notwithstanding the foregoing, GSK has retained its interest in the miR-122 program in HCV, and miR-122 remains a collaboration target under the alliance. If the HCV program is successful, we could receive contractual milestone payments up to $144.5 million, including up to $5.5 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 tiered royalties which can increase up to the low end of the 10 to 20% range on sales from any product that GSK successfully commercializes under this alliance.

We have evaluated the remaining contingent event-based payments under our strategic alliance agreement with GSK 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 collectability 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 collectability is reasonably assured. We can earn a preclinical milestone of $5.5 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.

Immuno-Inflammatory Alliance

The immuno-inflammatory alliance with GSK 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.

We have evaluated the remaining contingent event-based payments under our strategic alliance agreement with GSK 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 collectability 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 collectability is reasonably assured. We can earn the following preclinical milestones: $0.5 million 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.

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. Pursuant to the agreement, we granted 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 determined the elements within the strategic alliance agreement should be treated as a single unit of accounting because the delivered element, the license, does not have stand-alone value. As a result, we are recognizing revenue related to the upfront payment on a straight-line basis over our estimated period of performance, which is 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 $498.0 million, including up to $5.0 million for preclinical milestones, up to $123.0 million for clinical milestones, and up to

Table of Contents

$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 10 to 20%, 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 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 collectability 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 collectability is reasonably assured.

Concurrently with the collaboration and license agreement, we entered into a Common Stock Purchase Agreement (CSPA) with AstraZeneca, pursuant to which we agreed to sell to AstraZeneca an aggregate of $25.0 million of our common stock in a private placement concurrently with our initial public offering, at a price per share equal to the initial public offering price. In October 2012, in accordance with the CSPA, we sold AstraZeneca 6,250,000 shares of our common stock at a price per share of $4.00. Further, the CSPA stipulated that AstraZeneca could not sell, transfer, make any short sale of, or grant any option for the sale of any common stock for a 365-day period following the effective date of our initial public offering. Accounting guidance for multiple element arrangements contains a presumption that separate contracts negotiated and/or entered into at or near the same time with the same entity were negotiated as a package and should be evaluated as a single agreement. We valued the discount applied to the shares of common stock due to the one-year restriction. Based upon restricted stock studies of similar duration and a Black-Scholes valuation to measure the lack of marketability discount, $4.3 million was attributed to the collaboration and license agreement. We continue to recognize the $4.3 million into revenue ratably over the estimated period of performance of the collaboration.

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 (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. We also 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 $0.8 million. We are also eligible to receive research milestone payments up to an aggregate of $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 revenue relating to the upfront payment of $0.8 million on a straight-line basis over our estimated period of performance, which is approximately two years based on the expected term of the research and development plan.

In June 2013, we amended the collaboration and license agreement with Biogen Idec to provide for revised terms with respect to phase 1 of the research plan under the Biogen Idec agreement and revised payment provisions relating to the phase 1 milestones. The Biogen Idec amendment does not modify the maximum dollar amount we were originally eligible to receive in connection with phase 1 milestones under the Biogen Idec agreement, or our estimated period of performance.

We have evaluated the contingent event-based payments under our collaboration and license agreement with Biogen Idec 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 collectability is reasonably assured. We can earn the following research milestones: $0.25 million for identification of a *micro*RNA biomarker; $0.5 million for validation of the *micro*RNA biomarker in a second independent sample set; and $0.5 million upon the refinement of the *micro*RNA biomarker signature from 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 plus accrued interest 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.

Table of Contents

8. Related Party Transactions

We have entered into several agreements with related parties in the ordinary course of business to license intellectual property and to procure administrative and research and development support services. These agreements include a Services Agreement with our founding companies Isis Pharmaceuticals, Inc. (Isis) and Alnylam Pharmaceuticals, Inc. (Alnylam). Total costs incurred from services provided from Alnylam under the Services Agreement were $0.1 million and $0.5 million for the three and nine months ended September 30, 2013, respectively. Activities under the Services Agreement for the nine months ended September 30, 2012 were immaterial.

In August, 2013, we entered into an amendment to the Amended and Restated License and Collaboration Agreement with Isis and Alnylam dated January 1, 2009, as amended in June 2010 and October 2011 (as amended, the Amendment). Under the terms of the Amendment, the parties agreed to our use of certain Alnylam-controlled intellectual property concerning the use and manufacture of GalNAc conjugates (GalNAc Process Technology) on a non-exclusive basis. We will generally not be permitted to sublicense or otherwise transfer the GalNAc Process Technology and other Alnylam licensed intellectual property rights relating to GalNAc conjugate technology without the prior written consent of Alnylam, subject to certain limited exceptions for sublicenses to third party collaboration partners. There were no financial terms related to this Amendment.

9. Subsequent Events

In October 2013, we received a payment of $0.1 million from Biogen Idec for work performed pursuant to the terms of our collaboration and license agreement based on our research to discover *micro*RNAs as biomarkers for MS.

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, 2012 and the related Management s Discussion and Analysis of Financial Condition and Results of Operations for Regulus Therapeutics Inc., or we, us, our, or the Company, both of which are contained in our Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 19, 2013. Past operating results are not necessarily indicative of results that may occur in future periods.

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, beli estimate or other words indicating future results. 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, including our expected timeline for nominating clinical development candidates under our strategic alliances and our expected timeline for filing our first applications with regulatory authorities and potentially commencing Phase 1 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;

Table of Contents

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 Jumpstart Our Business Startups Act of 2012, or the JOBS Act;

our use of the proceeds from our initial public offering and concurrent private placement or subsequent public offerings; 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 *micro*RNAs to treat a broad range of diseases. We were formed in 2007 when Alnylam, and Isis contributed significant intellectual property, know-how and financial and human capital to pursue the development of drugs targeting *micro*RNAs pursuant to a license and collaboration agreement. *micro*RNAs are recently discovered, naturally occurring ribonucleic acid, or RNA, molecules that play a critical role in regulating key biological pathways. Scientific research has shown that the improper balance, or dysregulation, of *micro*RNAs is directly linked to many diseases. We believe we have assembled the leading position in the *micro*RNA field, including expertise in *micro*RNA 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 *micro*RNA product platform. 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. We are pursuing several *micro*RNA targets and are focusing our proprietary efforts in oncology and orphan diseases. We believe *micro*RNAs 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 several distinct programs, both independently and with our strategic alliance partners, AstraZeneca AB, or AstraZeneca, GlaxoSmithKline plc, or GSK, and Sanofi. We also have a collaboration agreement with Biogen Idec MA Inc., or Biogen Idec, to evaluate the potential use of *micro*RNA signatures as a biomarker for human patients with multiple sclerosis, or MS. Under these strategic alliances, we are eligible to receive up to approximately $1.3 billion in milestone payments upon successful commercialization of *micro*RNA therapeutics

for the programs contemplated by our agreements. These payments include up to $42.0 million upon achievement of preclinical and investigational new drug application, or IND, milestones, up to $272.0 million upon achievement of clinical development milestones, up to $305.0 million upon achievement of regulatory milestones and up to $670.0 million upon achievement of commercialization milestones.

We are currently executing on our Road to the Clinic Strategy which set forth certain corporate goals that seek to advance our *micro*RNA therapeutic pipeline toward the clinic. Specifically, we set the goal of nominating two *micro*RNA candidates for clinical development in 2013, be positioned to file our first applications with regulatory authorities by the first half of 2014 and maintain a strong year-end cash position to support these goals. In May 2013, we announced our first clinical candidate, RG-101, for which we have full ownership and commercial rights. RG-101 is a GalNAc-conjugated anti-miR, which targets microRNA-122, for the treatment of patients with chronic hepatitis C virus infection, or HCV. We expect to file our first application with regulatory authorities for RG-101 in the near term and potentially commence Phase 1 clinical trials of RG-101 in early 2014. Additionally, our strong financial position continues to support these stated goals and we continue to expect to end 2013 with approximately $110 million in cash, cash equivalents and short-term investments. Lastly, we anticipate that we will nominate a second *micro*RNA candidate for clinical development by the end of 2013, which we expect may come from our *micro*RNA-21 (miR-21) fibrosis program.

On July 22, 2013, we completed a public offering whereby we sold 5,175,000 shares of common stock at $9.50 per share and received net proceeds of $45.8 million, after deducting underwriting discounts, commissions and other offering expenses. On October 10, 2012, we completed our initial public offering whereby we issued and sold 11,250,000 shares of common stock at a public offering price of $4.00 per share, resulting in net proceeds to us of approximately $39.5 million. Concurrently with the completion of our initial public offering on October 10, 2012, $5.0 million of outstanding principal plus accrued interest of $0.8 million underlying a convertible note that we issued to GSK in April 2008 and amended and restated in July 2012, together with $5.0 million of outstanding principal plus accrued interest of $25,000 underlying a convertible note that we issued to Biogen Idec in August 2012, was automatically converted upon the closing of our initial public offering into an aggregate of 2,703,269 shares of our common stock. Upon the closing of our initial public offering, all shares of our outstanding convertible preferred stock automatically converted into an aggregate of 13,699,999 shares of common stock. On October 23, 2012, the underwriters for our initial public offering partially exercised an over-allotment option to purchase 1,480,982 shares of our common stock at $4.00 per share, resulting in net proceeds to us of approximately $5.5 million.

Table of Contents

Recent Developments

In November 2013, we presented positive new preclinical data demonstrating that miR-21 plays an important role in Alport Syndrome at the American Society of Nephrology s Kidney Week 2013 meeting. In a poster presentation, we and Genzyme, a Sanofi company, presented new preclinical data demonstrating that miR-21 plays an important role in the disease progression of Alport Syndrome in collagen 4A3 deficient mice. Treatment with an anti-miR-21 candidate significantly improved renal function, significantly reversed regulated genes and pathways associated with renal pathology, and increased the lifespan of the mice by 20 percent.

In November 2013, we presented positive data on RG-101, a GalNAc-conjugated anti-miR targeting miR-122 for the treatment of HCV, in a late-breaking poster at the 64th Annual American Association for the Study of Liver Diseases from preclinical studies evaluating RG-101 for *in vitro* and *in vivo* potency, pharmacokinetic/pharmacodynamics, toxicology and safety pharmacology and inhibition of HCV replication. Pharmacologic potency of RG-101 was significantly enhanced by approximately 20 fold *in vivo* in both mice and non-human primates, relative to the unconjugated oligonucleotide of RG-101. In addition to the potency studies, we tested the efficacy of RG-101 to reduce HCV viral load titer in a human chimeric liver mouse model infected with HCV and observed up to a 2 log reduction in HCV viral load titer with a single dose, which is similar to that observed for oral direct-acting antivirals as monotherapy in this mouse model. The duration of action observed for RG-101 supports the potential for a once-a-month dosing regimen. Additionally, RG-101 has demonstrated an excellent preclinical safety profile to date, although additional preclinical toxicology and safety pharmacology studies are currently ongoing.

In October 2013, we announced the selection of an undisclosed oncology target by AstraZeneca under the strategic alliance to discover, develop, and commercialize *micro*RNA therapeutics. We and AstraZeneca continue to collaborate on three exclusive *micro*RNA targets in cardiovascular and metabolic diseases and oncology.

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.

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;
- external research and development expenses incurred under arrangements with third parties, such as contract research organizations, or CROs, contract manufacturing organizations, or CMOs, consultants and our scientific advisory board;
- license 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. We are pursuing several *micro*RNA targets and focusing our proprietary efforts in oncology and orphan diseases. Our organization is structured to allow for 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 research and development personnel to 56 and have incurred approximately $88.6 million in research and development expenses through September 30, 2013.

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 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 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.

Table of Contents

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 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) consists primarily of interest income and expense, changes in convertible note payable valuation each reporting period, 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 has historically represented interest payable under convertible notes payable and equipment and tenant improvement financing arrangements.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

The preparation of our 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 believe that the estimates, assumptions and judgments involved in the accounting policies described in Management s Discussion and Analysis of Financial Condition and Results of Operations in Item 7 of our Annual Report on Form 10-K for the year ended December 31, 2012 have the greatest potential impact on our financial statements, so we consider them to be our critical accounting policies and estimates. There were no material changes to our critical accounting policies and estimates during the quarter ended September 30, 2013.

RESULTS OF OPERATIONS

The following table summarizes our results of operations for the periods indicated (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2013	2012	2013	2012
Revenue under strategic alliances	$ 6,118	$ 2,809	$ 14,115	$ 9,462
Research and development expenses	7,106	5,248	21,710	14,735

General and administrative expenses	1,917	1,093	5,545	2,998
Loss on extinguishment of debt		(1,738)		(1,738)
Gain (loss) from changes in valuation of convertible note payable	671	(331)	(3,787)	(331)

Revenue under strategic alliances

Our revenues are generated from ongoing strategic alliance and collaborations, and generally consist of upfront payments for licenses or options to obtain licenses in the future, research and development funding and milestone payments. The following table summarizes our total revenues for the periods indicated (in thousands):

Table of Contents

	Three months ended September 30,		Nine months ended September 30,	
	2013	2012	2013	2012
Sanofi	$ 5,422	$ 2,500	$ 10,828	$ 7,530
GSK	144	186	1,634	1,809
AstraZeneca	465	94	1,394	94
Biogen Idec	87	29	259	29
Total net revenues from research collaborators	$ 6,118	$ 2,809	$ 14,115	$ 9,462

Revenue under strategic alliances were $6.1 million and $14.1 million for the three and nine months ended September 30, 2013, compared to $2.8 million and $9.5 million for the same periods in 2012.

In June 2013, the research term expired under the Sanofi alliance, upon which we and Sanofi entered into an option agreement pursuant to which we granted Sanofi an exclusive right to negotiate the co-development and commercialization of certain of our unencumbered *micro*RNA programs and we were granted the exclusive right to negotiate with Sanofi for co-development and commercialization of certain miR-21 anti-miRs in oncology and Alport Syndrome. These options expire in December 2013, subject to a 30-day extension in certain circumstances. In addition, we agreed to continue specified research on the miR-21 programs during the option period. Upon the expiration of the research term and subsequent option agreement, we re-evaluated our estimated period of performance and are amortizing the remaining deferred revenue of $10.1 million associated with the initial upfront payment of $25.0 million ratably from June 2013 until the expiration of the option period in December 2013. As a result of the change in our estimated period of performance in June 2013, revenue recognized from the amortization of the upfront payment increased by $3.6 million and $3.9 million in the three and nine months ended September 30, 2013, compared to the three and nine months ended September 30, 2012.

In June 2013, the product development and commercialization agreement with GSK was amended to state that RG-101, and other formulations thereof, will be developed by us independently of our alliance with GSK for the treatment of chronic HCV infection. As a result, we accelerated the remaining unamortized deferred revenue of $1.1 million associated with the upfront payment from the February 2010 amendment that expanded our agreement with GSK to include potential *micro*RNA therapeutics for the treatment of HCV, due to the completion of our remaining performance obligations. As such, revenue of $0.1 million and $1.6 million was recognized for the three and nine months ended September 30, 2013.

In June 2012, we amended our product development and commercialization agreement with GSK to extend the target selection period for the fourth collaboration target under the agreement. As a result of the extension of the target selection period, we extended our estimated period of performance for the then remaining deferred revenue to approximately eight years, which represented our new estimated performance period under the amended agreement. Revenue of $0.2 million and $1.8 million was recognized for the three and nine months ended September 30, 2012.

In August 2012, we entered into a strategic alliance and concurrent Common Stock Purchase Agreement, or CPSA, with AstraZeneca. The strategic alliance included an upfront payment of $3.0 million and is being amortized over an estimated performance period of 48 months, which resulted in approximately $0.2 million and $0.6 million for the three and nine months ended September 30, 2013. In October 2012, pursuant to the CSPA, we sold AstraZeneca 6,250,000 shares of our common stock at a price per share of $4.00. Accounting guidance for multiple element arrangements contains a presumption that separate contracts negotiated and/or entered into at or near the same time with the same entity were negotiated as a package and should be evaluated as a single agreement. We valued the discount applied to the shares of common stock due to the one-year restriction. Based upon restricted stock studies of similar duration and a Black-Scholes valuation to measure the lack of marketability discount, $4.3 million was

attributed to the collaboration and license agreement, which is being amortized over the estimated period of performance of the collaboration. As such, revenue of $0.3 million and $0.8 million was recognized for the three and nine months ended September 30, 2013.

In August 2012, we entered into a collaboration and license agreement with Biogen Idec, which included an upfront payment of $0.8 million. We are recognizing revenue related to the upfront payment over our estimated period of performance, which is approximately two years. As such, revenue of $0.1 million and $0.3 million was recognized for the three and nine months ended September 30, 2013.

Research and development expenses

Research and development expenses were $7.1 million and $21.7 million for the three and nine months ended September 30, 2013, respectively, compared to $5.2 million and $14.7 million for the same periods in 2012. The increase was attributable to an expansion of our research and development personnel and increase in IND-enabling activities for RG-101. We expect our research and development expenses to increase over the coming quarters to the extent we commence clinical studies and initiate additional IND-enabling activities.

Table of Contents

General and administrative expenses

General and administrative expenses were $1.9 million and $5.5 million for the three and nine months ended September 30, 2013, respectively, compared to $1.1 million and $3.0 million for the same periods in 2012. The increase was primarily attributable to an increase in headcount, incremental operating expenses and other costs associated with being a public reporting company.

Loss on extinguishment of debt

In July 2012, we amended and restated our $5.0 million convertible promissory note originally issued in February 2010 to GSK, or the 2010 GSK Note, which resulted in a debt extinguishment for accounting purposes. As a result, we recognized a $1.7 million loss on extinguishment of debt in the three and nine months ended September 30, 2012.

Loss from valuation of convertible note payable

The amended and restated 2010 GSK Note provided for a rollover of the 2010 GSK Note into a new promissory note effective as of the closing date of a qualified initial public offering, or the Post-IPO GSK Note. We used a third party valuation firm to value the Post-IPO GSK Note at September 30, 2013 and 2012. Changes in the fair value of the Post-IPO GSK Note are recorded in non-operating earnings. We recorded a gain from the change in the valuation of the Post-IPO GSK Note of $0.7 million in the three months ended September 30, 2013, which was principally caused by a decrease in our stock price at September 30, 2013 compared to June 30, 2013. We recorded a loss from the change in the valuation of the Post-IPO GSK Note of $3.8 million for the nine months ended September 30, 2013, which was principally caused by an increase in our stock price at September 30, 2013 compared to December 31, 2012. We recorded a loss from the change in the valuation of the Post-IPO GSK Note of $0.3 million for the three and nine months ended September 30, 2012.

LIQUIDITY AND CAPITAL RESOURCES

Since our inception through September 30, 2013, we have received $66.3 million principally from upfront payments, research funding and preclinical milestones from our strategic alliances, collaborations, government grants and loans, and $170.7 million from the sale of our equity and convertible debt securities, including $70.0 million in net proceeds from our initial public offering and concurrent private placement of our common stock in October 2012 and $45.8 million in net proceeds from our public offering in July 2013. We expect that our existing cash and cash equivalents, together with interest and potential milestones, will be sufficient to fund our current operations into 2017. However, changing circumstances may cause us to consume capital more rapidly than we currently anticipate.

As of September 30, 2013, we had $123.9 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, 2013 and 2012 (in thousands):

	Nine months ended September 30,	
	2013	2012
	(Unaudited)	
Net cash provided by (used in):		
Operating activities	$ (19,016)	$ (9,572)
Investing activities	(34,524)	14,354
Financing activities	46,478	3,469

Total	$	(7,062)	$	8,251

Operating activities

Net cash used in operating activities increased to $19.0 million for the nine months ended September 30, 2013, compared $9.6 million for the nine months ended September 30, 2012. The increase in net loss to $16.7 million for the nine months ended September 30, 2013 from $10.5 million for the nine months ended September 30, 2012 included an increase of $3.5 million in non-cash charges associated with an increase in valuation of the Post-IPO GSK Note. Additionally, non-cash stock-based compensation charges increased by $1.8 million for the nine months ended September 30, 2013 compared to the nine months ended September 30, 2012. Changes in working capital resulted in a net increase in cash used in operating activities of $7.7 million for the nine months ended September 30, 2013 compared to the nine months ended September 30, 2012, principally as a result of a $11.1 million increase in the amortization of deferred revenue, offset by a decrease in contract and other receivables of $2.9 million.

Investing activities

Net cash provided by or used in investing activities for the periods presented primarily relate to the purchase, sale and maturity of investments used to fund the day-to-day needs of our business. In October 2012, we completed an initial public offering and concurrent private placement, resulting in net proceeds of $70.0 million, and in July 2013, we completed a public offering, resulting in net proceeds of $45.8 million. As such, net cash used in investing activities in the nine months ended September 30, 2013 included the net investment of short-term investments of $34.1 million. Conversely, net cash provided by investing activities in the nine months ended September 30, 2012 included the net maturity and sale of short term investments of $15.3 million.

Table of Contents

Financing activities

Net cash provided by financing activities was $46.5 million for the nine months ended September 30, 2013, compared to $3.5 million provided by financing activities for the nine months ended September 30, 2012. The change in cash from financing activities for the nine months ended September 30, 2013 was primarily due to $45.8 million in net proceeds from our public offering in July 2013. Net cash provided by financing activities for the nine months ended September 30, 2012 was a result of $5.0 million in proceeds from a convertible note issued by Biogen Idec in August 2012, offset by $1.3 million in payments related to our initial public offering.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

As of September 30, 2013, there were no material changes, outside of the ordinary course of business, in our outstanding contractual obligations from those disclosed within Management s Discussion and Analysis of Financial Condition and Results of Operations , as contained in our Annual Report on Form 10-K filed by us with the Securities and Exchange Commission, or the SEC, on February 19, 2013.

Off-Balance Sheet Arrangements

As of September 30, 2013, 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 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% change in interest rates were to have occurred on September 30, 2013, 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, 2013, 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, or the Exchange Act. 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, 2013.

Table of Contents

An evaluation was also performed under the supervision and with the participation of our management, including our chief executive officer and our principal financial officer, of any change in our internal control over financial reporting that occurred during our last fiscal quarter and that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting. That evaluation did not identify any change in our internal control over financial reporting that occurred during our latest fiscal quarter that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

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. The risk factors set forth below that are marked with an asterisk (*) contain changes to the similarly titled risk factors included in Item 1A of our Annual Report. If any of the following risks actually occurs, our business, financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock would likely decline.

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 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 $2.2 million and $5.7 million for the three months ended September 30, 2013 and 2012, respectively and $16.7 million and $10.5 million for the nine months ended September 30, 2013 and 2012, respectively. As of September 30, 2013, we had an accumulated deficit of $77.2 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 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.

Table of Contents

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;
- 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;
- 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 capital, 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 may need to raise additional capital 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 and potential milestones, will be sufficient to fund our current operations into 2017. 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 IND, and as we conduct clinical development of RG-101 and any other future product candidates, we may have adverse results requiring mitigation strategies that may cause us to consume additional capital. Additionally, 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 capital 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

Table of Contents

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.

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, 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. Any such increase, of the maximum amount or a lesser amount, will cause our stockholders to experience additional dilution, which could cause our stock price to fall. Currently, we plan to register the increased number of shares available for issuance under the 2012 Plan each year.

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.

Table of Contents

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.

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 or other regulatory authorities 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 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;

Table of Contents

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.

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.

Table of Contents

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;
- 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

Table of Contents

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.

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

Table of Contents

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, Sanofi may terminate the entire alliance or its current 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.

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, the GSK agreement or the 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, the GSK agreement or the 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.

Table of Contents

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;
- 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.

Table of Contents

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.

We, our alliance partners and our CROs are required to comply with the FDA s current good clinical practices, or 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 countries. There is no assurance that all of the potentially relevant prior art relating to our

patents and patent applications has been found; such prior art 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 initiated reexamination of 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

Table of Contents

that we or our strategic alliance partners may develop. 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, in certain situations, if we and one or more third parties have filed patent applications in the United States and claiming the same subject matter, an administrative proceeding can be initiated to determine which applicant is entitled to the patent on that subject matter. 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. 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.

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 each of our employees agrees to assign their inventions to us through an employee inventions agreement, 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. For example, we are aware that Santaris has patents and patent applications in the *micro*RNA therapeutics space, including patents and patent applications related to targeting *micro*RNAs, such as miR-122, for the treatment of disease. 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.

Table of Contents

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.

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.

Table of Contents

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., InteRNA Technologies B.V., miRagen Therapeutics, Inc., MiReven Pty Ltd, Mirna Therapeutics, Inc., and Santaris. Our competitors may 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 *micro*RNA 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.

Table of Contents

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;

Table of Contents

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;

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.

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

Market acceptance and sales of any future product candidates that we develop will depend on coverage and 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 coverage and adequate reimbursement will be available for any future product candidates. Also, inadequate reimbursement amounts may reduce the demand for, or the price of, our future products. If reimbursement is not available, or is available only at limited levels, we may not be able to successfully commercialize future product candidates that we develop.

In addition, 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. Obtaining formulary approval from hospitals and from payers can be an expensive and time consuming process. Failure to obtain timely formulary approval will limit our commercial success.

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.

In addition, in some non-U.S. jurisdictions, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the EU provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products. Historically, products launched in the EU do not follow price structures of the U.S. and generally tend to be priced significantly lower.

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.

Table of Contents

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

As of September 30, 2013, we had 69 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.

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.

Any future relationships with customers and third party payors may be subject, directly or indirectly, to federal and state healthcare fraud and abuse laws, false claims laws and health information privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers, subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The laws that may affect our ability to operate include:

the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs;

federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third party payers that are false or fraudulent;

the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;

HIPAA, as amended by the Health Information Technology and Clinical Health Act of 2009, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and

state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third party payer, including commercial insurers, and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

Table of Contents

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, possible exclusion from Medicare, Medicaid and other government healthcare programs, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

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.

RISKS RELATED TO OUR COMMON STOCK

The market price of our common stock may be highly volatile.*

Since shares of our common stock were sold in our initial public offering in October 2012 at a price of $4.00 per share, our closing stock price as reported on The NASDAQ Global Market has ranged from $4.15 to $12.41, through November 8, 2013. The trading price of our common stock is likely to continue to be volatile.

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;

Table of Contents

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 our preclinical and clinical development activities, product candidates or 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 September 30, 2013, our executive officers, directors, 5% stockholders and their affiliates beneficially owned approximately 69% 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.

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 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 through December 31, 2017, 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.

Table of Contents

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 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.*

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. Certain lock-up agreements pertaining to our recently completed public offering expired on October 14, 2013 and certain lock-up agreements pertaining to our initial public offering expired on October 4, 2013. Upon the expiration of these lock-up agreements, a substantial number of shares of common stock became eligible for sale in the public market, subject to volume limitations under Rule 144 under the Securities Act of 1933, as amended, or the Securities Act, with respect to any of these shares held by directors, executive officers and other affiliates. In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans are or may become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of our securities are entitled to rights with respect to the registration of their shares under 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 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.

Table of Contents

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.

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

None.

Use of Proceeds

On October 4, 2012, we commenced our initial public offering 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. Lazard Capital Markets, Cowen and Company and BMO Capital Markets acted as joint book-running managers for the offering, and Needham & Company and Wedbush PacGrow Life Sciences served as co-managers for the offering.

Table of Contents

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, 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.

As of November 8, 2013, 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 DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

Our policy governing transactions in our securities by directors, officers and employees permits our officers, directors and certain other persons to enter into trading plans complying with Rule 10b5-1 under the Exchange Act. We have been advised that certain of our directors and executive officers have entered into trading plans in accordance with Rule 10b5-1 and our policy governing transactions in our securities. Generally, under these trading plans, the individual relinquishes control over the transactions once the trading plan is put into place. Accordingly, sales under these plans may occur at any time, including possibly before, simultaneously with, or immediately after significant events involving the Company.

We anticipate that, as permitted by Rule 10b5-1 and our policy governing transactions in our securities, some or all of our officers, directors and employees may establish trading plans in the future. However, we undertake no obligation to update or revise the information provided herein, including for revision or termination of an established trading plan.

ITEM 6. EXHIBITS

Exhibit Number	Description

3.1	Amended and Restated Certificate of Incorporation of the Registrant (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 of the Registrant (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	Reference is made to Exhibits 3.1 and 3.2.
4.2	Form of Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.1 to 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	Amendment Number Three to the Amended and Restated License and Collaboration Agreement among the Company, Alnylam Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc., dated August 2, 2013 (incorporated by reference to Exhibit 99.1 to the Registrant s Current Report on Form 8-K, filed with the SEC on August 7, 2013).
31.1	Certification of the Principal Executive Officer and Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
32.1*	Certification of the Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

Table of Contents

Exhibit Number	Description
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 for 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.

* 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.

** Pursuant to applicable securities laws and regulations, we are deemed to have complied with the reporting obligation relating to the submission of interactive data files in such exhibits and are not subject to liability under any anti-fraud provisions of the federal securities laws as long as we have made a good faith attempt to comply with the submission requirements and promptly amend the interactive data files after becoming aware that the interactive data files fail to comply with the submission requirements. Users of this data are advised that, pursuant to Rule 460T, these interactive data files are deemed not filed and otherwise are not subject to liability.

Table of Contents

SIGNATURES

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

Regulus Therapeutics Inc.

Date: November 13, 2013

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

Table of Contents

EXHIBIT INDEX

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant (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 of the Registrant (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	Reference is made to Exhibits 3.1 and 3.2.
4.2	Form of Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.1 to 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	Amendment Number Three to the Amended and Restated License and Collaboration Agreement among the Company, Alnylam Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc., dated August 2, 2013 (incorporated by reference to Exhibit 99.1 to the Registrant s Current Report on Form 8-K, filed with the SEC on August 7, 2013).
31.1	Certification of the Principal Executive Officer and Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
32.1*	Certification of the Principal Executive Officer and Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted 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 for 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.

* 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.

** Pursuant to applicable securities laws and regulations, we are deemed to have complied with the reporting obligation relating to the submission of interactive data files in such exhibits and are not subject to liability under any anti-fraud provisions of the federal securities laws as long as we have made a good faith attempt to comply with the submission requirements and promptly amend the interactive data files after becoming aware that the interactive data files fail to comply with the submission requirements. Users of this data are advised that, pursuant

to Rule 460T, these interactive data files are deemed not filed and otherwise are not subject to liability.