Regulus Therapeutics Inc.
Form 10-Q
May 09, 2014
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**UNITED STATES**

**SECURITIES AND EXCHANGE COMMISSION**

**WASHINGTON, D.C. 20549**

# FORM 10-Q

**(Mark One)**

x **QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
**FOR THE QUARTERLY PERIOD ENDED MARCH 31, 2014**

**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 , smaller reporting company in Rule 12b-2 of the Exchange Act.

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

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

As of April 25, 2014, the registrant had 43,356,822 shares of Common Stock ($0.001 par value) outstanding.

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**REGULUS THERAPEUTICS INC.**

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## PART I. FINANCIAL INFORMATION

### ITEM 1. FINANCIAL STATEMENTS

**Regulus Therapeutics Inc.**

**CONDENSED BALANCE SHEETS**

**(in thousands, except share and per share data)**

| | March 31, 2014 (Unaudited) | December 31, 2013 |
|---|---|---|
| **Assets** | | |
| Current assets: | | |
| Cash and cash equivalents | $ 8,476 | $ 17,807 |
| Short-term investments | 106,121 | 96,198 |
| Contract and other receivables | 140 | 79 |
| Prepaid and other current assets | 3,492 | 3,098 |
| Total current assets | 118,229 | 117,182 |
| Property and equipment, net | 3,805 | 3,768 |
| Intangibles, net | 1,095 | 1,128 |
| Other assets | 978 | 987 |
| Total assets | $ 124,107 | $ 123,065 |
| **Liabilities and stockholders equity** | | |
| Current liabilities: | | |
| Accounts payable | $ 2,691 | $ 1,172 |
| Accrued liabilities | 3,279 | 3,013 |
| Accrued compensation | 859 | 1,297 |
| Current portion of deferred revenue | 2,739 | 4,888 |
| Total current liabilities | 9,568 | 10,370 |
| Convertible notes payable, at fair value | 13,403 | 11,279 |
| Deferred revenue, less current portion | 7,488 | 6,500 |
| Other long-term liabilities | 1,361 | 1,459 |
| Total liabilities | 31,820 | 29,608 |
| Stockholders equity: | | |
| Common stock, $0.001 par value; 200,000,000 shares authorized, 43,346,014 and 41,787,326 shares issued and outstanding at March 31, 2014 (unaudited) and December 31, 2013, respectively | 43 | 42 |
| Additional paid-in capital | 184,131 | 172,518 |
| Accumulated other comprehensive loss | (59) | (16) |

| | | |
|---|---|---|
| Accumulated deficit | (91,828) | (79,087) |
| Total stockholders equity | 92,287 | 93,457 |
| Total liabilities and stockholders equity | $ 124,107 | $ 123,065 |

See accompanying notes to these condensed financial statements.

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**Regulus Therapeutics Inc.**

**CONDENSED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS**

**(In thousands, except share and per share data)**

| | Three months ended March 31, | |
|---|---|---|
| | 2014 | 2013 |
| | (Unaudited) | |
| Revenues: | | |
| Revenue under strategic alliances and collaborations | $ 1,631 | $ 3,238 |
| Total revenues | 1,631 | 3,238 |
| Operating expenses: | | |
| Research and development | 9,604 | 6,883 |
| General and administrative | 2,732 | 1,905 |
| Total operating expenses | 12,336 | 8,788 |
| Loss from operations | (10,705) | (5,550) |
| Other income (expense): | | |
| Interest and other income | 100 | 72 |
| Interest expense | (11) | |
| Loss from valuation of convertible note payable | (2,124) | (1,761) |
| Loss before income taxes | (12,740) | (7,239) |
| Income tax expense (benefit) | 1 | (10) |
| Net loss | $ (12,741) | $ (7,229) |
| Other comprehensive loss: | | |
| Unrealized (loss) gain on short-term investments, net | (43) | 15 |
| Comprehensive loss | $ (12,784) | $ (7,214) |
| Net loss per share, basic and diluted | $ (0.30) | $ (0.20) |
| Shares used to compute basic and diluted net loss per share | 42,690,200 | 35,872,606 |

See accompanying notes to these condensed financial statements.

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**Regulus Therapeutics Inc.**

**Condensed Statements of Cash Flows**

**(In thousands)**

| | Three months ended March 31, | |
|---|---|---|
| | 2014 | 2013 |
| | (Unaudited) | |
| **Operating activities** | | |
| Net loss | $ (12,741) | $ (7,229) |
| Adjustments to reconcile net loss to net cash used in operating activities | | |
| Depreciation and amortization expense | 354 | 289 |
| Loss from valuation of convertible note payable | 2,124 | 1,761 |
| Stock-based compensation | 1,400 | 787 |
| Amortization of premium on investments, net | 443 | 324 |
| Gain on investments | (1) | (1) |
| Loss on disposal of long-term assets | 18 | 1 |
| Deferred income taxes | | (10) |
| Change in operating assets and liabilities: | | |
| Contracts and other receivables | (61) | |
| Prepaid and other current assets | (385) | (225) |
| Accounts payable | 1,519 | 86 |
| Accrued liabilities | (39) | 822 |
| Accrued compensation | (438) | (588) |
| Deferred revenue | (1,161) | (3,238) |
| Deferred rent and other liabilities | (61) | 66 |
| Net cash used in operating activities | (9,029) | (7,155) |
| **Investing activities** | | |
| Purchases of short-term investments | (39,780) | (18,074) |
| Maturities and sales of short-term investments | 29,372 | 2,430 |
| Purchases of property and equipment | (75) | (77) |
| Acquisition of intangibles | | (27) |
| Net cash used in investing activities | (10,483) | (15,748) |
| **Financing activities** | | |
| Proceeds from issuance of common stock, net | 9,728 | 85 |
| Principal payments on other long-term obligations | (34) | (28) |
| Proceeds from exercise of stock options | 487 | 116 |
| Net cash provided by financing activities | 10,181 | 173 |

| | | |
|---|---|---|
| Net decrease in cash and cash equivalents | (9,331) | (22,730) |
| Cash and cash equivalents at beginning of period | 17,807 | 40,552 |
| Cash and cash equivalents at end of period | $ 8,476 | $ 17,822 |
| **Supplemental disclosure of cash flow information** | | |
| Interest paid | $ 11 | $ |
| Income taxes paid | $ 1 | $ |
| **Supplemental disclosure of non-cash investing and financing activities** | | |
| Amounts accrued for property and equipment | $ 301 | $ 294 |
| Allowance for tenant improvements | $ | $ 482 |
| Amounts accrued for patent expenditures, net | $ | $ 15 |

See accompanying notes to these financial statements.

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**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 Company s audited financial statements and footnotes included in our Annual Report on Form 10-K for the year ended December 31, 2013, from which the balance sheet information herein was derived.

### 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

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

Multiple element arrangements, such as our strategic alliance agreements with Sanofi, AstraZeneca AB ( AstraZeneca ) and GlaxoSmithKline plc ( GSK ), are analyzed to determine whether the deliverables within the agreement can be separated or whether they must be accounted for as a single unit of accounting. Deliverables under the agreement will be accounted for as separate units of accounting provided that (i) a delivered item has value to the customer on a stand-alone basis; and (ii) if the agreement includes a general right of return relative to the delivered item, delivery or performance of the undelivered item is considered probable and substantially in the control of the vendor. The allocation of consideration amongst the deliverables under the agreement is derived using a best estimate of selling price if vendor specific objective evidence and third-party evidence of fair value is not available. If the delivered element does not have stand-alone value, the arrangement is then accounted for as a single unit of accounting, and we recognize the consideration received under the arrangement as revenue on a straight-line basis over our estimated

period of performance, which for us is often the expected term of the research and development plan.

*Milestones*

We apply the milestone method of accounting to recognize revenue from milestone payments when earned, as evidenced by written acknowledgement from the collaborator or other persuasive evidence that the milestone has been achieved and the payment is non-refundable, provided that the milestone event is substantive. A milestone event is defined as an event (i) that 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; (ii) for which there is substantive uncertainty at the inception of the arrangement that the event will be achieved; and (iii) that would result in additional payments being due to us. Events for which the occurrence is either contingent solely upon the passage of time or the result of a counterparty s performance are not considered to be milestone events. A milestone event is substantive if all of the following conditions are met: (i) the consideration is commensurate with either our performance to achieve the milestone, or the enhancement of the value to the delivered item(s) as a result of a specific outcome resulting from our performance to achieve the milestone; (ii) the consideration relates solely to past performance; and (iii) the consideration is reasonable relative to all the deliverables and payment terms (including other potential milestone consideration) within the arrangement.

We assess whether a milestone is substantive at the inception of each arrangement. If a milestone is deemed non-substantive, we will account for that milestone payment in accordance with the multiple element arrangements guidance and recognize revenue consistent with the related units of accounting for the arrangement over the related performance period.

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*Deferred Revenue*

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

**Stock-Based Compensation**

We account for stock-based compensation expense related to stock options granted to employees and members of our board of directors by estimating the fair value of each stock option on the date of grant using the Black-Scholes model. We recognize stock-based compensation expense using the accelerated multiple-option approach. Under the accelerated multiple-option approach (also known as the graded-vesting method), we recognize compensation expense over the requisite service period for each separately vesting tranche of the award as though the award was in substance multiple awards, resulting in accelerated expense recognition over the vesting period. For performance-based awards granted to employees (i) the fair value of the award is determined on the grant date, (ii) we assess the probability of the individual milestones under the award being achieved and (iii) the fair value of the shares subject to the milestone is expensed over the implicit service period commencing once management believes the performance criteria is probable of being met.

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

**Fair Value Option**

Applicable accounting policies permit entities to choose, at specified election dates, to measure specified items at fair value if the decision about the election is: 1) applied instrument by instrument, 2) irrevocable, and 3) applied to an entire instrument.

In July 2012, we amended and restated the $5.0 million convertible promissory note originally issued in February 2010 to GSK (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 difference between the carrying value of the 2010 GSK Note and the fair value of the amended and restated 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 amended note is recorded as gain (loss) from valuation of convertible note payable to non-operating earnings.

**Clinical Trial and Pre-Clinical Study Accruals**

We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on the facts and circumstances known to us at that time. Our accrued expenses for pre-clinical studies and clinical trials are based on estimates of costs incurred and fees that may be associated with services provided by clinical trial investigational sites and CROs. Payments under certain contracts with such parties depend on factors such as successful enrollment of patients, site initiation and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If possible, we obtain information regarding unbilled services directly from these service providers. However, we may be required to estimate these services based on other information available to us. If we underestimate or overestimate the activity or fees associated with a study or service at a given point in time, adjustments to research and development expenses may be necessary in future periods. Historically, our estimated accrued liabilities have

approximated actual expense incurred. Subsequent changes in estimates may result in a material change in our accruals.

**Recent Accounting Pronouncements**

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 adopted this guidance in 2014 and it did not 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 share equivalents outstanding for the period determined using the treasury-stock method. Dilutive common stock equivalents are comprised of options outstanding under our stock option plan and convertible notes payable. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to our net loss position.

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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 March 31, | |
|---|---|---|
| | 2014 | 2013 |
| Common stock options | 2,350,252 | 2,106,093 |
| Convertible note payable | 1,425,127 | 1,377,817 |
| Total | 3,775,379 | 3,483,910 |

For the three months ended March 31, 2014 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. As of March 31, 2014, 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):

| As of March 31, 2014 | Maturity (in years) | Amortized cost | Unrealized Gains | Unrealized Losses | Estimated fair value |
|---|---|---|---|---|---|
| Corporate debt securities | 2 or less | $ 86,225 | $ 31 | $ (58) | $ 86,198 |
| Certificates of deposit | 3 or less | 12,430 | | | 12,430 |
| Commercial paper | 1 or less | 7,492 | 1 | | 7,493 |
| Total | | $ 106,147 | $ 32 | $ (58) | $ 106,121 |

| As of December 31, 2013 | Maturity (in years) | Amortized cost | Unrealized Gains | Unrealized Losses | Estimated fair value |
|---|---|---|---|---|---|
| Corporate debt securities | 2 or less | $ 71,402 | $ 39 | $ (25) | $ 71,416 |
| Certificates of deposit | 2 or less | 11,710 | | | 11,710 |
| Commercial paper | 1 or less | 6,069 | 2 | | 6,071 |
| Debt securities of U.S. government-sponsored agencies | 1 or less | 7,000 | 1 | | 7,001 |
| Total | | $ 96,181 | $ 42 | $ (25) | $ 96,198 |

**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.

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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 March 31, 2014 and December 31, 2013 (in thousands):

| | Fair value as of March 31, 2014 | | | |
|---|---|---|---|---|
| | Total | Level 1 | Level 2 | Level 3 |
| Assets: | | | | |
| Cash equivalents | $ 7,340 | $ 7,340 | $ | $ |
| Corporate debt securities | 86,198 | | 86,198 | |
| Certificates of deposit | 12,430 | | 12,430 | |
| Commercial paper | 7,493 | | 7,493 | |
| | $ 113,461 | $ 7,340 | $ 106,121 | $ |
| Liabilities: | | | | |
| Convertible notes payable | $ 13,403 | $ | $ | $ 13,403 |

| | Fair value as of December 31, 2013 | | | |
|---|---|---|---|---|
| | Total | Level 1 | Level 2 | Level 3 |
| Assets: | | | | |
| Cash equivalents | $ 17,170 | $ 17,170 | $ | $ |
| Corporate debt securities | 71,416 | | 71,416 | |
| Certificates of deposit | 11,710 | | 11,710 | |
| Debt securities of U.S. government-sponsored agencies | 7,001 | | 7,001 | |
| Commercial paper | 6,071 | | 6,071 | |
| | $ 113,368 | $ 17,170 | $ 96,198 | $ |
| Liabilities: | | | | |
| Convertible notes payable | $ 11,279 | $ | $ | $ 11,279 |

Changes in the estimated fair value of convertible notes payable from December 31, 2013 through March 31, 2014 are as follows (in thousands):

| | Fair Value Measurements Using Significant Unobservable Inputs |
|---|---|

| | | (Level 3) |
|---|---|---|
| Balance at December 31, 2013 | $ | 11,279 |
| Change in estimated fair value of convertible notes payable | | 2,124 |
| Balance at March 31, 2014 | $ | 13,403 |

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.

We used an income approach in the form of a convertible bond valuation model to value the convertible notes payable. The convertible bond model considered the debt and option characteristics of the note. The key inputs to the model as of March 31, 2014 and December 31, 2013 were volatility (65% and 66%, respectively), risk-free rate (0.26% and 0.325%, respectively), and credit spread (7.4% and 7.4%, respectively). The volatility inputs were based on historical and implied volatility of peer companies. Peer companies were materially consistent with those used to determine volatility for stock-based compensation. Beginning in 2014, our historical volatility was included with the peer companies for purposes of estimating volatility. The risk-free rate inputs were based on the yield of US Treasury Strips as of each date. The credit spread inputs were based on an analysis of our creditworthiness and market rates for comparable straight debt instruments. We recorded a loss from the change in valuation of convertible notes payable of $2.1 million and $1.8 million on the condensed statements of operations and comprehensive loss for the three months ended March 31, 2014 and 2013, respectively.

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**5. Convertible Notes Payable**

In October 2012, in conjunction with our initial public offering the amended and restated 2010 GSK Note provided for a rollover into a new promissory note (the Post-IPO GSK Note ), and the Post-IPO GSK Note was established in the principal amount of $5.4 million, with a maturity date of October 9, 2015. At GSK s option, the Post-IPO GSK Note is convertible into shares of our common stock at any time prior to the maturity date with a conversion equal to the quotient of all outstanding principal and interest divided by our initial public offering price of $4.00 per share, subject to complying with certain threshold ownership percentage limitations. At March 31, 2014 and December 31, 2013, the fair value of the Post-IPO Note was $13.4 million and $11.3 million, respectively, and is classified as Convertible note payable, at fair value on the condensed balance sheets.

**6. Stockholders Equity**

**Shares Reserved for Future Issuance**

The following shares of common stock are reserved for future issuance at March 31, 2014:

| | March 31, 2014 |
|---|---|
| Common stock options outstanding | 5,815,877 |
| Common stock options available for future grant | 1,928,980 |
| Employee Stock Purchase Plan | 858,625 |
| Convertible note payable | 1,425,127 |
| Total common shares reserved for future issuance | 10,028,609 |

The following table summarizes our stock option activity under all stock option plans for the three months ended March 31, 2014 (in thousands):

| | Number of options | Weighted average exercise price |
|---|---|---|
| Options outstanding at December 31, 2013 | 5,598 | $ 3.69 |
| Granted | 500 | $ 8.44 |
| Exercised | (235) | $ 2.07 |
| Canceled/forfeited/expired | (47) | $ 4.72 |
| Options outstanding at March 31, 2014 | 5,816 | $ 4.15 |

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**Stock-Based Compensation**

The following table summarizes the weighted average assumptions used to estimate the fair value of stock options and performance stock awards granted under our 2012 Equity Incentive Plan and the shares purchasable under the 2012 Employee Stock Purchase Plan:

| | Three months ended March 31, | |
|---|---|---|
| | 2014 | 2013 |
| **Stock options** | | |
| Risk-free interest rate | 1.9% | 1.2% |
| Volatility | 74.0% | 67.3% |
| Dividend yield | 0% | 0% |
| Expected term (years) | 6.1 | 6.1 |
| **Performance stock options** | | |
| Risk-free interest rate | 2.2% | |
| Volatility | 70.1% | |
| Dividend yield | 0% | |
| Expected term (years) | 6.4 | |
| **Employee stock purchase plan shares** | | |
| Risk-free interest rate | 0.1% | 0.1% |
| Volatility | 65.2% | 59.7% |
| Dividend yield | 0% | 0% |
| Expected term (years) | 0.5 | 0.5 |

The following table summarizes the allocation of our stock-based compensation expense for all stock awards (in thousands):

| | Three months ended March 31, | |
|---|---|---|
| | 2014 | 2013 |
| Research and development | $ 804 | $ 499 |
| General and administrative | 596 | 288 |
| Total | $ 1,400 | $ 787 |

**7. Strategic Alliances and Collaborations**

The following table summarizes our total net revenues from our strategic alliances and collaborations (in thousands):

| | Three months ended March 31, | |
|---|---|---|
| | 2014 | 2013 |

| | | |
|---|---|---|
| Sanofi | $ 925 | $ 2,500 |
| GSK | 144 | 187 |
| AstraZeneca | 465 | 465 |
| Biogen Idec | 87 | 86 |
| Other | 10 | |
| Total | $ 1,631 | $ 3,238 |

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**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. 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 Sanofi was granted 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. 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. Revenue associated with the creditable portion of this payment remained deferred as of March 31, 2014, and will remain deferred until its application to a creditable transaction. The non-creditable portion of this payment, $1.25 million, was recognized as revenue over the option period from the effective date of the option agreement in June 2013 through the expiration of the option period in January 2014.

In conjunction with the option agreement, we agreed to continue specified research on the miR-21 programs during the option period. We re-evaluated our remaining estimated period of performance from the original research term through the term of the option agreement and amortized the remaining deferred revenue of $10.1 million associated with the initial $25.0 million upfront payment from June 2013 through the expiration of the option period in January 2014.

In February 2014, we and Sanofi entered into a second amended and restated collaboration and license agreement (the 2014 Sanofi Amendment ) to renew our strategic alliance to discover, develop and commercialize *micro*RNA therapeutics to focus on specific orphan disease and oncology targets. Under the terms of our renewed alliance, Sanofi will have opt-in rights to our preclinical fibrosis program targeting miR-21 for the treatment of Alport Syndrome, our preclinical program targeting miR-21 for oncology indications, and our preclinical program targeting miR-221/222 for hepatocellular carcinoma ( HCC ). We are responsible for developing each of these programs to proof-of-concept, at which time Sanofi has an exclusive option on each program. If Sanofi chooses to exercise its option on any of these programs, Sanofi will reimburse us for a significant portion of our preclinical and clinical development costs and will also pay us an option exercise fee for any such program, provided that $1.25 million of the $2.5 million upfront option fee paid to us by Sanofi in connection with the June 2013 option agreement will be creditable against such option exercise fee. In addition, we will be eligible to receive clinical and regulatory milestone payments and potentially commercial milestone payments for these programs. We also continue to be eligible to receive royalties on *micro*RNA therapeutic products commercialized by Sanofi and will have the right to co-promote these products.

In connection with the 2014 Sanofi Amendment, we entered into a Common Stock Purchase Agreement (the Purchase Agreement ), pursuant to which we sold 1,303,780 shares of our common stock to Aventis Holdings, Inc. ( Aventis ), an entity affiliated with Sanofi, in a private placement at a price per share of $7.67 for an aggregate purchase price of $10.0 million. Under the terms of the Purchase Agreement, Aventis may not sell, transfer, make any short sale of, or grant any option for the sale of any common stock issued pursuant to the Purchase Agreement for a 12-month period following its effective date. The Purchase Agreement and the 2014 Sanofi Amendment were negotiated concurrently and were therefore evaluated as a single agreement. Based upon restricted stock studies of similar duration and a Black-Scholes valuation to measure the discount for lack of marketability, approximately $0.4 million of the proceeds

from the Purchase Agreement was attributed to the 2014 Sanofi Amendment, and represents the value of the program targeting miR-221/222 target for HCC. As this element does not have stand-alone value, we are recognizing the $0.4 million into revenue ratably over the estimated period of performance of the miR-221/222 program. As of March 31, 2014, deferred revenue associated with the Purchase Agreement and the 2014 Sanofi Amendment was $0.4 million, which we are expecting to recognize over the remaining estimated period of performance of approximately six years.

We have evaluated the remaining contingent event-based payments under our 2014 Sanofi Amendment and determined that event-based payments for which payment is contingent upon the results of Sanofi s performance will be recognized as revenue over our remaining estimated period of performance, if any, and when collectability is reasonably assured. We are eligible to receive milestone payments of up to $101.8 million for proof-of-concept option exercise fees (net of $1.25 million creditable, as noted above), $15.0 million for clinical milestones and up to $300.0 million for regulatory and commercial milestones. In addition, we are entitled to receive royalties based on a percentage of net sales of any products from the miR-21 and miR-221/222 programs which, in the case of sales in the United States, will be in the middle of the 10 to 20% range, and, in the case of sales outside of the United States, will range from the low end to the middle of the 10 to 20% range, depending upon the volume of sales. If we exercise our option to co-promote a product, we will continue to be eligible to receive royalties on net sales of each product in the United States at the same rate, unless we elect to share a portion of Sanofi s profits from sales of such product in the United States in lieu of royalties.

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**GSK**

In April 2008, we entered into a strategic alliance with GSK to discover, develop and commercialize novel *micro*RNA-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 *micro*RNA therapeutics targeting miR-122 for the treatment of HCV (the HCV alliance ). In June 2012, we amended our immuno-inflammatory alliance to extend the target selection period for the fourth collaboration target. We determined that the elements within the immuno-inflammatory 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 period of performance. As of March 31, 2014, deferred revenue associated with the immuno-inflammatory alliance was $3.4 million, which we are expecting to recognize over the remaining estimated period of performance of approximately six years.

In June 2013, the HCV alliance was amended to state that RG-101, and other formulations thereof, will be developed by us independently of our alliance for the treatment of HCV. This amendment removed any further milestone or royalty obligations owed by GSK to us as it relates to RG-101. Concurrently with the amendment in June 2013, we recorded the remaining $1.1 million in deferred revenue associated with the upfront payment from the HCV alliance, as our estimated period of performance was complete.

*Immuno-Inflammatory Alliance*

Under the terms of the immuno-inflammatory alliance, 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 immuno-inflammatory alliance and determined that the preclinical and clinical payments meet the definition of a substantive milestone. 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.

*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. We are also entitled to 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 the HCV alliance and determined that the preclinical and clinical payments meet the definition of a substantive milestone. 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. We have no obligation to perform any research or development activities unless mutually agreed upon by the parties.

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**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 preclinical milestones of up to $5.0 million upon lead compound identification, up to $123.0 million for clinical milestones, and up to $370.0 million for commercialization milestones. In addition, we are entitled to receive royalties based on a percentage of net sales which will range from the mid-single digits to the low end of 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. 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 a discount for lack of marketability, $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. As of March 31, 2014, deferred revenue associated with the

collaboration and license agreement and CSPA was $4.4 million, which we are expecting to recognize over the remaining contractual term and corresponding estimated period of performance of approximately 2.5 years.

**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 original expected term of the research and development plan.

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Concurrently with the collaboration and license agreement, we entered into a note purchase agreement with Biogen Idec, pursuant to which we issued 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.

In June 2013, we amended the collaboration and license agreement to provide for revised terms with respect to Phase I of the research plan and related milestone payment provisions. The Biogen Idec amendment does not modify the maximum dollar amount we were originally eligible to receive in connection with Phase I 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. Accordingly, revenue for these achievements will be recognized in its entirety in the period when the milestone is achieved and collectability is reasonably assured. In October 2013 and November 2013, we received research milestone payments totaling $0.3 million. In addition, we can earn the following research milestones: $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. As of March 31, 2014, deferred revenue associated with the collaboration and license agreement was $0.2 million, which we are expecting to recognize over the remaining estimated period of performance of 7 months.

**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.

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. Pursuant to our Amended and Restated Services Agreement with Alnylam dated January 1, 2009, we purchased GalNAc-related materials from Alnylam in the three months ended March 31, 2013.

The following table summarizes the amounts included in our operating expenses as a result of costs incurred from services provided under the Services Agreement (in thousands):

| | Three months ended March 31, | |
|---|---|---|
| | 2014 | 2013 |
| Services performed or out-of-pocket expenses paid to Alnylam | $ | $ 355 |

**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, 2013 and the related Management s Discussion and Analysis of Financial Condition and Results of Operations, both of which are contained in our Annual Report on Form 10-K for the year ended December 31, 2013, or Annual Report, filed with the Securities and Exchange Commission on February 28, 2014. 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 and the documents incorporated by reference herein 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 current expectations or beliefs concerning various future events, may contain words such as may, will, expect, anticipate, intend, plan, believe, estimate or other words indicating future results. Such statem 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;

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our ability to obtain and maintain regulatory approval of our future product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;

our ability to obtain funding for our operations;

our plans to research, develop and commercialize our future product candidates;

our strategic alliance partners election to pursue development and commercialization;

our ability to attract collaborators with development, regulatory and commercialization expertise;

our ability to obtain and maintain intellectual property protection for our future product candidates;

the size and growth potential of the markets for our future product candidates, and our ability to serve those markets;

our ability to successfully commercialize our future product candidates;

the rate and degree of market acceptance of our future product candidates;

our ability to develop sales and marketing capabilities, whether alone or with potential future collaborators;

regulatory developments in the United States and foreign countries;

the performance of our third-party suppliers and manufacturers;

the success of competing therapies that are or become available;

the loss of key scientific or management personnel;

our ability to successfully secure and deploy capital;

our ability to satisfy our debt obligations;

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 our subsequent public offering in July 2013;

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

the additional risks and other factors described under the caption Risk Factors under Item 1A of this quarterly report on Form 10-Q.

**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. We have established strategic alliances with AstraZeneca, GSK and Sanofi to discover, develop and commercialize *micro*RNA therapeutics. Under these strategic alliances, we are eligible to receive up to approximately $1.5 billion in milestone payments upon successful commercialization of *micro*RNA therapeutics for the programs contemplated by our agreements. These payments include up to $128.0 million upon achievement of preclinical and IND milestones, up to $254.0 million upon achievement of clinical development milestones, up to $380.0 million upon achievement of regulatory milestones and up to $730.0 million upon achievement of commercialization milestones.

*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 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.

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In addition to our *micro*RNA product platform, we have established Regulus *micro*Markers , a research and development division focused on identifying *micro*RNAs as biomarkers of human disease to support our therapeutic pipeline, collaborators and strategic partners. Regulus *micro*Markers utilizes a clinically-validated, highly reproducible, proprietary technology platform to identify *micro*RNAs as potential biomarkers for disease and we control key intellectual property and know-how related to the division. We believe that *micro*RNA biomarkers are of significant value and may be used to select optimal patient segments for our clinical trials and the clinical trials of our strategic alliance partners and collaborators. We have a research collaboration with Biogen Idec MA Inc. to identify *micro*RNA biomarkers for multiple sclerosis, and more recently, we entered into an arrangement with another leading, commercial-stage pharmaceutical company to explore *micro*RNAs as biomarkers for specific patient populations.

Currently, we are pursuing several *micro*RNA targets across multiple therapeutic areas to advance our therapeutics pipeline, with a primary focus on orphan diseases and oncology, both independently and with our strategic alliance partners. In February 2014, we launched our Clinical Map Initiative , which outlines certain corporate goals and objectives to advance our *micro*RNA therapeutic pipeline over the next several years. Recently, we commenced dosing human subjects in our first clinical trial, a Phase I study of our wholly owned compound, RG-101, a GalNac-conjugated anti-miR targeting microRNA-122 ( miR-122 ) for the treatment of hepatitis C virus infection ( HCV ). Under our Initiative , we intend to demonstrate human proof-of-concept results in the Phase I clinical study of RG-101 by the end of 2014. Also recently, we nominated our second microRNA candidate for clinical development, RG-012, an anti-miR targeting microRNA-21 ( miR-21 ) for the treatment of Alport Syndrome, a life-threatening kidney disease driven by genetic mutations with no approved therapy. We expect to initiate a Phase I clinical study of RG-012 for the treatment of Alport Syndrome in the first half of 2015 and to nominate a third *micro*RNA candidate for clinical development by the end of 2014. Additionally, we expect to maintain a strong financial position and end 2014 with at least $75.0 million in cash, cash equivalents and short-term investments.

**FINANCIAL OPERATIONS OVERVIEW**

**Revenues**

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

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

**Research and development expenses**

Research and development expenses consist of costs associated with our research activities, including our drug discovery efforts, the development of our therapeutic programs, and our Regulus *micro*Markers™ division. 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.

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

Since our conversion to a corporation in January 2009, we have grown from 15 research and development personnel to 59 and have spent a total of approximately $106.4 million in research and development expenses through March 31, 2014.

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

Most of our product development programs are at an early stage, and successful development of future product candidates from these programs is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each future product candidate and are difficult to predict. We anticipate 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, and on occasion income or expense of a non-recurring nature, including changes in the valuation of convertible notes payable from period to period. 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 and under Note 1 to our financial statements contained in our Annual Report 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 March 31, 2014.

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**RESULTS OF OPERATIONS**

**Comparison of the three months ended March 31, 2014 and 2013**

The following table summarizes our results of operations for the three months ended March 31, 2014 and 2013, together with the changes in those items in dollars (in thousands):

| | Three months ended March 31, | | |
|---|---|---|---|
| | 2014 | 2013 | Increase/(Decrease) |
| Revenue under strategic alliances | $ 1,631 | $ 3,238 | $ (1,607) |
| Research and development expenses | 9,604 | 6,883 | 2,721 |
| General and administrative expenses | 2,732 | 1,905 | 827 |
| Loss from changes in valuation of convertible note payable | (2,124) | (1,761) | 363 |

*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):

| | Three months ended March 31, | |
|---|---|---|
| | 2014 | 2013 |
| Sanofi | $ 925 | $ 2,500 |
| GSK | 144 | 187 |
| AstraZeneca | 465 | 465 |
| Biogen Idec | 87 | 86 |
| Other | 10 | |
| Total net revenues from strategic alliances | $ 1,631 | $ 3,238 |

Revenue under strategic alliances was $1.6 million for the three months ended March 31, 2014, compared to $3.2 million for the three months ended March 31, 2013. Our revenue during these periods consisted primarily of amortization of upfront payments received from the Sanofi, GSK and AstraZeneca strategic alliances, which we amortize monthly on a straight-line basis over our estimated period of performance.

Revenue recognized from our Sanofi strategic alliance was $0.9 million for the three months ended March 31, 2014 compared to $2.5 million for the three months ended March 31, 2013. This decrease was primarily due to the expiration of the research term under the Sanofi alliance in June 2013. Revenue associated with payments received from Sanofi under the research program was $1.25 million in the three months ended March 31, 2013. Revenue associated with the amortization of other payments received from Sanofi was $0.9 million and $1.25 million for the three months ended March 31, 2014 and 2013, respectively. Revenue from our other strategic alliances was materially consistent for the three months ended March 31, 2014 compared to the three months ended March 31, 2013.

As of March 31, 2014, we had $10.2 million of deferred revenue, which consists of payments received through our strategic alliances, but have not yet recognized in accordance with our revenue recognition policies and remaining estimated period of performance.

*Research and development expenses*

Research and development expenses were $9.6 million for the three months ended March 31, 2014 compared to $6.9 million for the three months ended March 31, 2013. This increase was primarily driven by the initiation of a Phase I clinical study for RG-101 and the continued advancement of other pre-clinical programs totaling $3.4 million for the three months ended March 31, 2014, compared to pre-clinical development costs of $0.8 million for the three months ended March 31, 2013. We had 59 employees engaged in research and development activities as of March 31, 2014, compared to 57 as of March 31, 2013. We expect our research and development expenses to continue to increase to the extent we continue clinical studies and initiate additional pre-clinical and clinical programs.

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*General and administrative expenses*

General and administrative expenses were $2.7 million for the three months ended March 31, 2014 compared to $1.9 million for the three months ended March 31, 2013. This increase was primarily driven by an increase in salaries and related employee costs of $0.2 million and an increase in operating costs of $0.6 million associated with general business activities.

*Loss from valuation of convertible note payable*

We recorded a loss from changes in value of convertible notes payable of $2.1 million and $1.8 million in the statements of operations and comprehensive loss for the three months ended March 31, 2014 and 2013, respectively. Changes in value were primarily driven by increases in our stock price during the respective periods.

**LIQUIDITY AND CAPITAL RESOURCES**

Since our inception through March 31, 2014, we have received $65.5 million principally from upfront payments, research funding and preclinical milestones from our strategic alliances and collaborations, $180.8 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 $2.5 million from government grants and loans.

As of March 31, 2014, we had $114.6 million in cash, cash equivalents and short-term investments. The following table shows a summary of our cash flows for the three months ended March 31, 2014 and 2013 (in thousands):

| | Three months ended March 31, | |
|---|---|---|
| | 2014 | 2013 |
| | (unaudited) | |
| Net cash (used in) provided by: | | |
| Operating activities | $ (9,029) | $ (7,155) |
| Investing activities | (10,483) | (15,748) |
| Financing activities | 10,181 | 173 |
| Total | $ (9,331) | $ (22,730) |

*Operating activities*

Net cash used in operating activities was $9.0 million for the three months ended March 31, 2014, compared to $7.2 million for the three months ended March 31, 2013. The increase in net cash used in operating activities was attributable in part to a net loss to $12.7 million for the three months ended March 31, 2014 compared to a net loss of $7.2 million for the three months ended March 31, 2013. Adjustments for non-cash charges increased by $1.2 million for the three months ended March 31, 2014, primarily as a result of a $0.6 million increase in stock-based compensation and $0.4 million increase associated with the loss in valuation of the Post-IPO GSK Note. Changes in working capital resulted in net cash used in operating activities of $0.6 million for the three months ended March 31, 2014, compared to $3.1 million for the three months ended March 31, 2013. This reduction was primarily driven by the amortization of deferred revenue associated with upfront payments, compared to the period of revenue

recognition.

*Investing activities*

Net cash used in investing activities for the periods presented primarily relate to the net of purchases, sales and maturities of investments used to fund the day-to-day needs of our business. We invest cash in excess of our immediate operating requirements in such a way that maturity is staggered to optimize our return on investment, while satisfying the liquidity needs of the company. As such, for the three months ended March 31, 2014 and 2013, net cash used in investing activities primarily reflects the net purchase of short-term investments, offset by sales and maturities. The net purchases of short-term investments were $10.4 million and $15.6 million for the three months ended March 31, 2014 and 2013, respectively.

*Financing activities*

Net cash provided by financing activities was $10.2 million for the three months ended March 31, 2014, compared to $0.2 million for the three months ended March 31, 2013. The increase in net cash provided by financing activities is primarily a result of the 2014 Sanofi Amendment and concurrent Common Stock Purchase Agreement with Aventis, which was completed in February 2014, and included a private placement of our common stock with proceeds of $9.6 million, which excludes $0.4 million in proceeds from the private placement attributed to the 2014 Sanofi Amendment.

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## CONTRACTUAL OBLIGATIONS AND COMMITMENTS

There have been 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.

### Off-Balance Sheet Arrangements

As of March 31, 2014, 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 March 31, 2014, 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 is 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 March 31, 2014, we carried out an evaluation, under the supervision and with the participation of our management, including our chief executive officer and principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the

Securities Exchange Act of 1934, as amended. Based on this evaluation, our chief executive officer and principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of March 31, 2014.

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.

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## 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 $12.7 million and $7.2 million for the three months ended March 31, 2014 and 2013, respectively. As of March 31, 2014, we had an accumulated deficit of $91.8 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 relating to the development of our miR-21 programs for HCC and kidney fibrosis and our miR-221/222 program for oncology indications, with GSK to develop our miR-122 program for HCV, and with AstraZeneca, to develop metabolic and oncology programs. Under our agreements with Sanofi and GSK, Sanofi and GSK each have an option to obtain exclusive worldwide licenses for the development, manufacture and commercialization of potential product candidates selected from our programs. If either of Sanofi or GSK exercises their respective options to obtain a license to develop, manufacture and commercialize such product candidates, such party will assume responsibility for funding and conducting further clinical development and commercialization activities for such product candidates. However, if either of these parties does not exercise its option within the timeframes that we expect, or at all, we will be responsible for funding further development of the applicable 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 only recently initiated clinical development of any product candidate and it will be several years, if ever, before we have a product candidate ready for commercialization. Even if we or our strategic alliance partners successfully obtain regulatory approval to market a product candidate, our revenues will also depend upon the size of any markets in which our product candidates have received market approval, and our ability to achieve sufficient market acceptance and adequate market share for our products.

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

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

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

identifying and validating new *micro*RNAs as therapeutic targets;

completing our research and preclinical development of future product candidates;

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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 will need to raise additional capital to support our operations and such funding may not be available to us on acceptable terms, or at all.

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, RG-012 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
- 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.

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**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.

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

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

The success of our future product candidates will depend on several factors, including the following:

successful completion of preclinical studies and clinical trials;

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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;

be subject to additional post-marketing testing requirements; or

have the product removed from the market after obtaining marketing approval.

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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 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.

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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

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other programs or product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and future product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic alliance, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

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

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

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 alliances with Sanofi and GSK, Sanofi and GSK each have the option to obtain an exclusive worldwide license to develop, manufacture and commercialize product candidates upon the achievement of relevant endpoints in clinical trials. However, neither Sanofi nor GSK is under any obligation to exercise these options 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;

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- an alliance partner may exercise its rights under the agreement to terminate a strategic alliance;

- an alliance partner may be acquired by another company and the acquiring company may not devote sufficient resources to the collaboration, or may terminate the collaboration;

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

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

Specifically, with respect to termination rights, 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.

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

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

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

- the inability to meet any product specifications and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- a failure to comply with cGMP and similar foreign standards;
- 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 or miR-221/222 for oncology indications or RG-012 for kidney fibrosis under its strategic alliance with us, Sanofi will be responsible for the manufacture of the product candidates for further 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

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such a case, we will have no control over Sanofi s processes or supply chains to ensure the timely manufacture and supply of the product candidates. In addition, we will not be able to ensure that the product candidates will be manufactured under the correct conditions to permit the product candidates to be used in such clinical trials. Each of AstraZeneca and GSK will have similar obligations to manufacture product candidates which it takes into clinical trials under its strategic alliance with us and we will face similar risks as to those product candidates.

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

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

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

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

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

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.

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## 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 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 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 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, as well as administrative proceedings including interferences, inter partes review and oppositions before the U.S. Patent and Trademark Office, or U.S. PTO, and 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

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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 patents that our future product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our future product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patents were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

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

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

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.

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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.

**RISKS RELATED TO COMMERCIALIZATION OF PRODUCT CANDIDATES**

**The commercial success of our programs that are part of our strategic alliance agreements with Sanofi, GSK and AstraZeneca, will depend in large part on the development and marketing efforts of our alliance partners. If our alliance partners are unable or unwilling 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., Microlin Bio, 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.

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Most of our programs 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.

**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. For example, we have co-promotion rights with Sanofi with respect to our miR-21 and

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miR-221/222 programs, but would need to build our sales, marketing, managerial and other non-technical capabilities in order to effectively carry out co-promotion activities with respect to any approved products that are developed through these programs. With respect to certain of our current programs that are the subject of existing strategic alliances, such as miR-122 with GSK and the metabolic and oncology programs 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 their respective programs, as applicable. If any other future product candidates that we may develop are approved for commercialization, we may also enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;

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.

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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.

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

As of March 31, 2014, we had 74 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

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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.

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;

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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 maintain product liability insurance relating to the use of our therapeutics in clinical trials. However, such insurance 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.

**Cyber security risks and the failure to maintain the confidentiality, integrity, and availability of our computer hardware, software, and Internet applications and related tools and functions could result in damage to our reputation and/or subject us to costs, fines or lawsuits.**

Our business requires manipulating, analyzing and storing large amounts of data. In addition, we rely on a global enterprise software system to operate and manage our business. We also maintain personally identifiable information about our employees. Our business therefore depends on the continuous, effective, reliable, and secure operation of our computer hardware, software, networks, Internet servers, and related infrastructure. To the extent that our hardware or software malfunctions or access to our data by internal research personnel is interrupted, our business could suffer. The integrity and protection of our employee and Company data is critical to our business and employees have a high expectation that we will adequately protect their personal information. The regulatory environment governing information, security and privacy laws is increasingly demanding and continues to evolve. Maintaining compliance with applicable security and privacy regulations may increase our operating costs. Although our computer and communications hardware is protected through physical and software safeguards, it is still vulnerable to fire, storm, flood, power loss, earthquakes, telecommunications failures, physical or software break-ins, software viruses, and similar events. These events could lead to the unauthorized access, disclosure and use of non-public information. The techniques used by criminal elements to attack computer systems are sophisticated, change frequently and may originate from less regulated and remote areas of the world. As a result, we may not be able to address these techniques proactively or implement adequate preventative measures. If our computer systems are compromised, we could be subject to fines, damages, litigation and enforcement actions, and we could lose trade secrets, the occurrence of which could harm our business. In addition, any sustained disruption in internet access provided by other

companies could harm our 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 April 25, 2014. 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;

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any delay in filing an IND or NDA for any of our future product candidates and any adverse development or perceived adverse development with respect to the FDA s review of that IND or NDA;

failure to maintain our existing strategic alliances or enter into new alliances;

failure of our strategic alliance partners to elect to develop and commercialize product candidates under our alliance agreements or the termination of any programs under our alliance agreements;

failure by us or our licensors and strategic alliance partners to prosecute, maintain or enforce our intellectual property rights;

failure to successfully develop and commercialize our future product candidates;

changes in laws or regulations applicable to 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 April 25, 2014, our executive officers, directors, 5% stockholders and their affiliates beneficially owned approximately 77% 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

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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.

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 July 2013 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 connection with our private placement of 1,303,780 shares to Aventis Holdings Inc., or Aventis, an entity affiliated with Sanofi, in February 2014, Aventis has agreed that for a period of 12 months after the date on which the shares were issued, subject to specified exceptions, Aventis will not offer, sell, contract to sell, pledge or otherwise dispose of, directly or indirectly, any of the shares of our common stock issued to Aventis in the private placement. Subject to certain limitations, all of the shares issued to Aventis in the private placement will become eligible for sale upon expiration of the lock-up period. 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. We filed a registration statement that became effective on April 16, 2014, which provides for the sale of up to 8,600,000 shares of common stock by the selling stockholders named therein. In addition, we may file additional registration statements in the future to provide for the further sale of shares of common stock by our stockholders. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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**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. We have filed a registration statement that provides for the sale of up to $100 million of common stock or warrants by us from time to time in one or more public offerings. The registration statement became effective on April 16, 2014. 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. In addition, we may file additional registration statements in the future to provide for the further sale of shares of common stock by us or by selling 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.

**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;

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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 $51.8 million. 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 $50.9 million. 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.

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 March 31, 2014, we have used approximately $15.3 million of the net proceeds from the offering 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 intend to use some or all of the remaining proceeds for similar uses, and we may also use a portion of the remaining 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 remaining net proceeds from our initial public offering. Accordingly, our management will continue to have broad discretion in the application of the remaining net proceeds.

**ITEM 3. DEFAULTS UPON SENIOR SECURITIES**

None.

**ITEM 4. MINE SAFETY DISCLOSURE**

Not applicable.

**ITEM 5. OTHER INFORMATION**

None.

**ITEM 6. EXHIBITS**

For a list of exhibits filed with this quarterly report on Form 10-Q, refer to the exhibit index.

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**SIGNATURES**

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

Regulus Therapeutics Inc.

Date: May 8, 2014

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

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## 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+ | Employment Agreement between the Registrant and David Szekeres, dated February 4, 2014. |
| 10.2 | Second Amended and Restated Collaboration and License Agreement dated February 4, 2014 between the Registrant and Sanofi (incorporated by reference to Exhibit 10.52 to the Registrant s Annual Report on Form 10-K, filed with the SEC on February 28, 2014). |
| 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. |

+ Indicates management contract.
We have requested confidential treatment for certain portions of this agreement, which have been omitted and filed separately with the SEC pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, 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, as amended, 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.