Regulus Therapeutics Inc.
Form 10-Q
November 06, 2015
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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q

(Mark One)

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

FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2015

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

858-202-6300
(Registrant's Telephone Number, Including Area Code)

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

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨

Indicate by check mark whether registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer", "accelerated filer", and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	¨	Accelerated filer	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 ¨ No ý

As of October 30, 2015, the registrant had 52,342,653 shares of Common Stock ($0.001 par value) outstanding.

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PART I. FINANCIAL INFORMATION

ITEMS 1. FINANCIAL STATEMENTS

Regulus Therapeutics Inc.
CONDENSED BALANCE SHEETS
(in thousands, except share and per share data)

	September 30, 2015 (Unaudited)	December 31, 2014
Assets		
Current assets:		
Cash and cash equivalents	$18,324	$37,327
Short-term investments	112,002	122,416
Restricted cash	1,400	—
Contract and other receivables	325	274
Prepaid and other current assets	4,759	4,934
Total current assets	136,810	164,951
Property and equipment, net	3,488	3,568
Intangibles, net	1,072	1,150
Other assets	2,077	1,811
Total assets	$143,447	$171,480
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$3,392	$2,188
Accrued liabilities	7,409	4,402
Accrued compensation	1,999	2,108
Current portion of deferred revenue	2,009	3,097
Convertible note payable, at fair value	—	23,397
Total current liabilities	14,809	35,192
Deferred revenue, less current portion	2,083	3,252
Other long-term liabilities	693	1,022
Total liabilities	17,585	39,466
Stockholders' equity:		
Common stock, $0.001 par value; 200,000,000 shares authorized, 52,342,653 and 48,944,530 shares issued and outstanding at September 30, 2015 (unaudited) and December 31, 2014, respectively	52	49
Additional paid-in capital	310,233	267,929
Accumulated other comprehensive loss	(134)	(197)
Accumulated deficit	(184,289)	(135,767)
Total stockholders' equity	125,862	132,014
Total liabilities and stockholders' equity	$143,447	$171,480

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 September 30,		Nine months ended September 30,	
	2015	2014	2015	2014
	(Unaudited)			
Revenues:				
Revenue under strategic alliances and collaborations	$1,865	$1,083	$9,899	$3,450
Total revenues	1,865	1,083	9,899	3,450
Operating expenses:				
Research and development	10,965	10,173	43,593	30,572
General and administrative	4,245	2,569	13,703	8,255
Total operating expenses	15,210	12,742	57,296	38,827
Loss from operations	(13,345)	(11,659)	(47,397)	(35,377)
Other income (expense):				
Interest and other income	335	86	686	283
Interest expense	(6)	(10)	(22)	(31)
Gain (loss) from valuation of convertible note payable	—	1,785	(1,811)	614
Loss before income taxes	(13,016)	(9,798)	(48,544)	(34,511)
Income tax benefit (expense)	16	—	22	(1)
Net loss	$(13,000)	$(9,798)	$(48,522)	$(34,512)
Other comprehensive loss:				
Unrealized gain (loss) on short-term investments, net	40	(24)	96	(50)
Comprehensive loss	$(12,960)	$(9,822)	$(48,426)	$(34,562)
Net loss per share:				
Basic	$(0.25)	$(0.23)	$(0.95)	$(0.80)
Diluted	$(0.25)	$(0.26)	$(0.95)	$(0.80)
Weighted average shares used to compute net loss per share:				
Basic	51,990,460	43,406,251	51,052,068	43,155,601
Diluted	51,990,460	44,855,463	51,052,068	43,155,601

See accompanying notes to these condensed financial statements.

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Regulus Therapeutics Inc.
CONDENSED STATEMENTS OF CASH FLOWS
(In thousands)

	Nine months ended September 30,	
	2015	2014
	(Unaudited)	
Operating activities		
Net loss	$(48,522)	$(34,512)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization expense	1,177	1,098
Loss (gain) from valuation of convertible note payable	1,811	(614)
Stock-based compensation	11,607	4,710
Amortization of premium on investments, net	1,130	1,235
Loss on disposal of long-term assets	73	18
Change in operating assets and liabilities:		
Contracts and other receivables	(50)	50
Prepaid and other current assets	(91)	(882)
Accounts payable	1,024	1,470
Accrued liabilities	1,649	610
Accrued compensation	(109)	147
Deferred revenue	(2,257)	(980)
Deferred rent and other liabilities	(257)	(203)
Net cash used in operating activities	(32,815)	(27,853)
Investing activities		
Purchases of short-term investments	(67,064)	(52,268)
Sales and maturities of short-term investments	76,411	63,074
Purchases of property and equipment	(873)	(1,120)
Acquisition of intangibles	(40)	(53)
Net cash provided by investing activities	8,434	9,633
Financing activities		
Proceeds from issuance of common stock, net	492	9,853
Proceeds from exercise of common stock options	5,001	624
Principal payments on other long-term obligations	(115)	(106)
Net cash provided by financing activities	5,378	10,371
Net decrease in cash and cash equivalents	(19,003)	(7,849)
Cash and cash equivalents at beginning of period	37,327	17,807
Cash and cash equivalents at end of period	$18,324	$9,958
Supplemental disclosure of cash flow information		
Restricted cash received	$1,400	$—
Interest paid	$(22)	$(30)
Income taxes paid	$(1)	$(1)
Supplemental disclosure of non-cash investing and financing activities		
Amounts accrued for property and equipment, net	$179	$—

See accompanying notes to these condensed 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, 2014, from which the balance sheet information herein was derived.

Use of Estimates

Our condensed financial statements are prepared in accordance with GAAP, which 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. An estimated loss contingency is accrued in our financial statements if it is probable that a liability has been incurred and the amount of the loss can be reasonably estimated. 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, milestone payments and payments for other research services under strategic alliance and collaboration agreements. We recognize revenues when all four of the following criteria are met: (1) persuasive evidence of 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 and AstraZeneca AB ("AstraZeneca") and our collaboration agreement with Biogen Inc. ("Biogen"), formerly Biogen Idec MA Inc., 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

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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 using a method consistent with the related units of accounting for the arrangement over the related performance period.

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 option pricing 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 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 Glaxo Group Limited (“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 was recorded as gain (loss) from valuation of convertible note payable to non-operating earnings.

The amended and restated 2010 GSK Note provided for a rollover into a new promissory note, effective as of the closing date of a qualifying initial public offering (the “Post-IPO GSK Note”). In October 2012, upon our initial public offering, the Post-IPO GSK Note was established in the principal amount of $5.4 million, which was equivalent to the original principal amount of $5.0 million plus accrued but unpaid interest of approximately $0.4 million. The 2010 GSK Note was simultaneously cancelled and obligations thereunder were terminated. In January 2015, the principal balance of the Post-IPO GSK Note was converted into common stock.

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, clinical research organizations (“CROs”) and for other clinical trial-related activities. 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 for these services, 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 activities or fees

associated with a study or service at a given point in time, adjustments to research and

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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.

Restricted Cash

Restricted cash consists of amounts received for a specific and limited purpose, and therefore not available for general operating activities. In August 2015, we received $1.4 million in connection with our facility lease agreement with Walton Torrey Owner B, L.L.C, entered into in July 2015. The use of these funds are restricted to costs associated with the relocation of our corporate headquarters.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-9, Revenue from Contracts with Customers (“ASU 2014-19”). Adoption of ASU No. 2014-9 requires that an entity recognize revenue to depict the transfer of goods or services to customers in an amount that reflects the consideration to which the entity expects to be entitled in exchange for those goods or services. This update is effective for annual reporting periods beginning after December 15, 2017 and interim periods therein and requires expanded disclosures. We are currently evaluating the impact of adoption on our financial position, results of operations and cash flows.

In August 2014, the FASB issued ASU No. 2014-15, Presentation of Financial Statements Going Concern, which requires management to assess an entity’s ability to continue as a going concern, and to provide related footnote disclosure in certain circumstances. This standard is effective for annual reporting periods ending after December 15, 2016 and interim periods thereafter. Early application is permitted. The adoption of this guidance will have no impact on our financial position, results of operations or cash flows.

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 plans and convertible note payable, which was converted into common stock in January 2015.

Applicable accounting standards provide that a contract convertible into common stock that is reported as an asset or liability for accounting purposes may require an adjustment to the numerator of the diluted earnings per share calculation for any changes in income or loss that would result if the contract had been reported as an equity instrument during the period. Securities are assumed to be converted at the beginning of the period, and the resulting common shares are included in the denominator of the diluted earnings per share calculation for the entire period presented. Adding back the gain from the change in valuation of the convertible note payable for the three months ended September 30, 2014 to the numerator and adding the number of shares to be issued upon conversion of the convertible note payable into the denominator of the diluted earnings per share calculation resulted in an increase to the loss per share for the period. The impact of the conversion to the numerator and denominator for the nine months ended September 30, 2014 was anti-dilutive, and therefore was excluded. There is no difference in net loss or the number of shares used to calculate basic and diluted shares outstanding for the three and nine months ended September 30, 2015.

The following table summarizes the adjustment to net loss for the diluted net loss per share calculation for the three months ended September 30, 2014 (in thousands):

Net loss	$(9,798)
Less: gain from change in valuation of note payable	1,785
Net loss used to compute diluted net loss per share	$(11,583)

The following table summarizes the adjustment to weighted average shares outstanding for the diluted net loss per share calculation for the three months ended September 30, 2014 (in common equivalent shares):

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Weighted average shares outstanding used for basic net loss per share	43,406,251
Plus: weighted average shares of convertible note payable	1,449,212
Weighted average shares outstanding used for diluted net loss per share	44,855,463

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

	Three months ended September 30,		Nine months ended September 30,	
	2015	2014	2015	2014
Common stock options	2,269,605	1,949,096	2,499,389	2,313,182
Convertible note payable	—	—	—	1,449,212
Total	2,269,605	1,949,096	2,499,389	3,762,394

3. Investments

We invest our excess cash in commercial paper and debt instruments of financial institutions and corporations. As of September 30, 2015, our short-term investments had a weighted average maturity of less than two years.

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

	Maturity (in years)	Amortized cost	Unrealized Gains	Losses	Estimated fair value
As of September 30, 2015					
Corporate debt securities	2 or less	$93,192	$12	$(81)	$93,123
Certificates of deposit	2 or less	15,080	—	—	15,080
Commercial paper	1 or less	3,798	1	—	3,799
Total		$112,070	$13	$(81)	$112,002

	Maturity (in years)	Amortized cost	Unrealized Gains	Losses	Estimated fair value
As of December 31, 2014					
Corporate debt securities	2 or less	$105,085	$2	$(167)	$104,920
Certificates of deposit	2 or less	14,600	—	—	14,600
Commercial paper	1 or less	2,895	1	—	2,896
Total		$122,580	$3	$(167)	$122,416

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.

Accounting standards define 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 accounting standards provide 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

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would use in valuing the asset or liability. The accounting standards prioritize the inputs used in measuring the fair value into the following hierarchy:

- Level 1 includes financial instruments for which quoted market prices for identical instruments are available in active markets.
- Level 2 includes financial instruments for which there are inputs other than quoted prices included within Level 1 that are observable for the instrument such as quoted prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets with insufficient volume or infrequent transactions (less active markets) or model-driven valuations in which significant inputs are observable or can be derived principally from, or corroborated by, observable market data.
- Level 3 includes financial instruments for which fair value is derived from valuation techniques in which one or more significant inputs are unobservable, including management's own assumptions.

The following table presents our fair value hierarchy for assets and liabilities measured at fair value on a recurring basis as of September 30, 2015 and December 31, 2014 (in thousands):

	Fair value as of September 30, 2015			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$16,830	$16,830	$—	$—
Corporate debt securities	93,123	—	93,123	—
Certificates of deposit	15,080	—	15,080	—
Commercial paper	3,799	—	3,799	—
	$128,832	$16,830	$112,002	$—

	Fair value as of December 31, 2014			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$37,072	$37,072	$—	$—
Corporate debt securities	104,920	—	104,920	—
Certificates of deposit	14,600	—	14,600	—
Commercial paper	2,896	—	2,896	—
	$159,488	$37,072	$122,416	$—
Liabilities:				
Convertible note payable	$23,397	$—	$—	$23,397

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. Refer to Note 3 for information regarding our investments.

The following table presents a reconciliation of the liability measured at fair value using significant unobservable inputs (Level 3) from December 31, 2014 to September 30, 2015 (in thousands):

	Fair Value Measurements Using Significant Unobservable Inputs (Level 3)
Balance at December 31, 2014	$ 23,397
Change in estimated fair value of convertible note payable	1,811
Convertible note converted to shares of common stock	(25,208)
Balance at September 30, 2015	$ —

We used an income approach in the form of a convertible bond valuation model to value the convertible note payable. The convertible bond model considered the debt and option characteristics of the note. The key inputs to the model as

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December 31, 2014 were volatility of 110%, risk-free rate of 0.10% and credit spread of 9.7%. 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. As of December 31, 2014, the volatility input included 60% weighting of our historical volatility and 40% weighting of historical and implied volatility of peer companies. 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. On January 29, 2015, the principal balance of the convertible note payable was converted into 1,356,738 shares of common stock, at a conversion price of $4.00 per share. A final valuation upon conversion at January 29, 2015 was performed, considering only the option characteristics of the note as its conversion was certain. Key inputs of volatility, risk-free rate and credit spread were considered, however, the final valuation was substantially driven by the number of shares of common stock issued upon conversion (1,356,738) and our stock price on the date of conversion ($18.58). Upon issuance of the common stock, the fair value of the convertible note was classified into stockholders' equity.

We recorded a loss from the change in valuation of the convertible note payable of zero and $1.8 million on the condensed statements of operations and comprehensive loss for the three and nine months ended September 30, 2015, respectively. We recorded a gain of $1.8 million and $0.6 million for the three and nine months ended September 30, 2014.

5. Convertible Note Payable

In October 2012, in conjunction with our initial public offering the amended and restated 2010 GSK Note was rolled over into a new promissory 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 December 31, 2014, the fair value of the Post-IPO GSK Note was $23.4 million and was classified as “Convertible note payable, at fair value” on the condensed balance sheets. On January 29, 2015, the principal amount outstanding under the Post-IPO GSK Note of $5.4 million was converted into 1,356,738 shares of our common stock at a conversion price of $4.00 per share.

6. Stockholders’ Equity

Shares Reserved for Future Issuance

The following shares of common stock were reserved for future issuance as of September 30, 2015:

Common stock options outstanding	5,781,674
Common stock available for future grant	2,177,821
Employee Stock Purchase Plan	1,260,136
Total common shares reserved for future issuance	9,219,631

The following table summarizes our stock option activity under all equity incentive plans for the nine months ended September 30, 2015 (shares in thousands):

	Number of options	Weighted average exercise price
Options outstanding at December 31, 2014	6,643	$6.95
Granted	1,776	$11.23
Exercised	(1,984)	$2.58
Canceled/forfeited/expired	(653)	$11.28
Options outstanding at September 30, 2015	5,782	$9.27

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 to employees under our 2012 Equity Incentive Plan and 2015 Inducement Plan and the shares purchasable under our 2012 Employee Stock Purchase Plan during the periods presented:

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	Three months ended September 30,		Nine months ended September 30,	
	2015	2014	2015	2014
Stock options				
Risk-free interest rate	1.7%	2.0%	1.8%	1.9%
Volatility	78.9%	70.1%	78.8%	73.0%
Dividend yield	—	—	—	—
Expected term (years)	6.1	6.1	6.1	6.1
Performance stock options				
Risk-free interest rate	1.6%	—	1.8%	2.1%
Volatility	79.3%	—	76.7%	69.6%
Dividend yield	—	—	—	—
Expected term (years)	6.1	0	6.0	6.3
Employee stock purchase plan shares				
Risk-free interest rate	0.2%	0.1%	0.1%	0.1%
Volatility	77.1%	71.3%	75.6%	69.4%
Dividend yield	—	—	—	—
Expected term (years)	0.5	0.5	0.5	0.5

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

	Three months ended September 30,		Nine months ended September 30,	
	2015	2014	2015	2014
Research and development	$1,048	$890	$6,500	$2,548
General and administrative	1,586	737	5,107	2,162
Total	$2,634	$1,627	$11,607	$4,710

7. Strategic Alliances and Collaborations

The following table summarizes our total revenues from our strategic alliances and collaborations during the periods presented (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2015	2014	2015	2014
AstraZeneca	$1,380	$465	$8,028	$1,394
Sanofi	18	18	54	961
GSK	—	144	—	433
Biogen	467	449	1,817	622
Other	—	7	—	40
Total	$1,865	$1,083	$9,899	$3,450

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 microRNA 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

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research, development and manufacturing activities described in the research plan, at our cost, until the acceptance of an investigational new drug application ("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 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.

In March 2015, we earned a $2.5 million preclinical milestone payment upon AstraZeneca's selection of RG-125, a GalNAc-conjugated anti-miR targeting microRNA-103/107, as a lead compound under the agreement. If all three targets are successfully developed and commercialized through pre-agreed sales targets, we could receive additional milestone payments of up to $495.5 million, including preclinical milestones of up to $2.5 million upon selection of a lead compound, 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 the 10 to 20% range, depending upon the product and the volume of sales, which royalties may be reduced in certain, limited circumstances.

In January 2015, we entered into a letter agreement with AstraZeneca to amend the collaboration and license agreement. Under the terms of the letter agreement, we have agreed to perform additional miR-103/107 program research and development activities related to RG-125. AstraZeneca has agreed to fund 50% of the costs for these additional activities, as outlined in the letter agreement. In accordance with the collaboration and license agreement, AstraZeneca will fund 100% of the costs for product manufacturing activities outlined in the letter agreement necessary to support a Phase I clinical study. We have recognized $0.9 million and $4.1 million for the three and nine months ended September 30, 2015, respectively, for the performance of research and development and product manufacturing activities outlined in the letter agreement. As of September 30, 2015, deferred revenue from advanced payments associated with the letter agreement was $0.4 million, which we will recognize in the period services are provided.

We have evaluated the contingent event-based payments under our collaboration and license 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 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 standards 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 September 30, 2015, deferred revenue associated with the

collaboration and license agreement and CSPA was $1.6 million, which we are expecting to recognize over the remaining contractual term and corresponding estimated period of performance of approximately one year.

Sanofi

In July 2012, we amended and restated our collaboration and license agreement with Sanofi to expand the potential therapeutic applications of the microRNA 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 microRNA targets; and (2) a research license under our technology alliance.

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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 microRNA 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 option payment remained deferred as of September 30, 2015, 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 microRNA 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 microRNA 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 Aventisub LLC (formerly 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 was not permitted to sell, transfer, make any short sale of, or grant any option for the sale of any common stock for the 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 consideration for the value of the program targeting miR-221/222 for HCC. As this element does not have stand-alone value, we are recognizing the $0.4 million allocated consideration into revenue ratably over the estimated period of performance of the miR-221/222 program. As of September 30, 2015, deferred revenue associated with the Purchase Agreement and the 2014 Sanofi Amendment was $0.3 million, which we are expecting to recognize over the remaining estimated period of performance of approximately four years.

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.

We have evaluated the contingent event-based payments under the 2014 Sanofi Amendment and determined that the milestone payments meet the definition of substantive milestones. Accordingly, revenue for these achievements will be recognized in their entirety in the period when the milestone is achieved and collectability is reasonably assured. Other contingent event-based payments under the 2014 Sanofi Amendment for which payment is contingent upon the results of Sanofi's performance will not be accounted for using the milestone method. Such payments will be recognized as revenue over the remaining estimated period of performance, if any, and when collectability is reasonably assured.

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GSK

In April 2008, we entered into a strategic alliance with GSK to discover, develop and commercialize novel microRNA-targeted therapeutics to treat inflammatory diseases (the "immuno-inflammatory alliance"). In February 2010, we and GSK expanded the strategic alliance to include hepatitis C virus infection ("HCV") to discover, develop and commercialize microRNA therapeutics targeting miR-122 for the treatment of HCV (the "HCV alliance"). In June 2012, we amended our 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 microRNA 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.

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, 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.

In October 2014, we received written notice from GSK of its election to terminate the product development and commercialization agreement. Concurrently with the notice of termination, we recorded the remaining $3.1 million in deferred revenue associated with the upfront payment, as our estimated period of performance was complete. The effective date of the termination was January 15, 2015.

Biogen

In August 2012, we entered into a collaboration and license agreement with Biogen pursuant to which we and Biogen agreed to collaborate on microRNA biomarkers for multiple sclerosis ("MS"). Under the terms of the agreement, in August 2012 we received an upfront payment of $0.8 million. We were also eligible to receive research milestone payments of 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, did not have stand-alone value. As a result, we recognized revenue relating to the upfront payment of $0.8 million on a straight-line basis over our estimated period of performance, which was approximately two years based on the expected term of the research and development plan.

In June 2013, we amended the collaboration and license agreement to provide for revised terms with respect to the initial phase of the research plan and related milestone payment provisions. The amendment did not modify the maximum dollar amount we were originally eligible to receive in connection with the agreement, or our estimated period of performance. In October 2013 and November 2013, we received research milestone payments totaling $0.3 million under the August 2012 collaboration and license agreement.

In August 2014, we entered into a new collaboration and license agreement with Biogen to collaborate on microRNA biomarkers for MS and simultaneously executed an agreement terminating the August 2012 collaboration and license agreement. As a result of the termination agreement, we recognized $0.1 million in deferred revenue associated with the upfront payment, as our estimated period of performance was complete. Pursuant to the terms of the August 2014 collaboration and license agreement, we received an upfront payment of $2.0 million. We determined that the elements within the August 2014 collaboration and license agreement were to be treated as a single unit of accounting because the delivered element, the license, did not have stand-alone value to Biogen. As a result, we recognized revenue relating to the upfront payment of $2.0 million on a straight-line basis over the estimated period of performance, which was approximately one year based on the expected term of the research and development plan.

In July 2015, the collaboration and license agreement was amended to modify the conditions of the third research-based milestone. Additionally, the amendment extended the expected research term from 12 months to 14 months. We recognized the remaining upfront payment on a straight-line basis over the amended expected term. As of September 30, 2015, our period of performance was complete and the deferred revenue balance was zero.

In January 2015, May 2015, and September 2015, we earned research milestone payments under the August 2014 collaboration and license agreement of $0.1 million, $0.3 million and $0.3 million, respectively. We have evaluated the contingent event-based payments under our collaboration and license agreement with Biogen and determined that the research milestone payments met the definition of substantive milestones. Accordingly, revenue for these achievements was recognized in the period the milestones were achieved and collectability was reasonably assured.

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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 February 2015, we entered into a letter agreement with Alnylam Pharmaceuticals, Inc. ("Alnylam") pursuant to which we and Alnylam agreed to the financial terms for certain technology acquired by Alnylam within the licensed patent rights under our Amended and Restated License and Collaboration Agreement (the “Additional Patent Rights”) with Alnylam and Isis Pharmaceuticals, Inc. ("Isis"). In addition to any royalties payable by us to Alnylam pursuant to the terms of the Amended and Restated License and Collaboration Agreement, we agreed to pay Alnylam an additional low single-digit royalty on net sales of certain products utilizing the Additional Patent Rights, with the exact royalty percentage payable being dependent on the total amount of net sales during the calendar year. We also agreed to pay Alnylam milestone payments on certain products utilizing the additional patent rights of up to $33.0 million per product upon the achievement of certain regulatory milestone events. There was no activity under this agreement for the three or nine months ended September 30, 2015.

In September 2014, we entered into an agreement with Sanofi-Aventis Deutschland GmbH (“Sanofi Deutschland”), a contract manufacturing subsidiary of Sanofi, for the manufacture of certain drug substance requirements and other services to support our preclinical and clinical activities associated with the RG-012 program. Pursuant to this agreement, we may engage Sanofi Deutschland from time-to-time to manufacture RG-012 drug product on our behalf. Expenses incurred under the Sanofi agreement for services performed or out-of-pocket expenses were zero and $0.4 million for the three and nine months ended September 30, 2015, respectively.

9. Subsequent Events

In October 2015, we provided written notice to BMR - John Hopkins Court LLC of our election to exercise our early termination option under our current facility lease. The termination will be effective June 30, 2016. Fees associated with our exercise of this early termination option were not material.

In October 2015, we entered into a Clinical Trial Collaboration and Formulation Development Agreement ("Clinical Trial Collaboration") with GlaxoSmithKline LLC ("GSK LLC") to evaluate the combination of RG-101, our wholly-owned GalNAc-conjugated anti-miR targeting microRNA-122, and GSK2878175, GSK LLC's non-nucleoside NS5B polymerase inhibitor in a Phase II clinical study. Under the terms of the Clinical Trial Collaboration, each party will provide drug compound for use in the clinical trial. All other costs of the Phase II clinical study will be incurred by the Company. Concurrently, GSK LLC will work on developing a long-acting parenteral formulation for injection ("LAP") of GSK2878175, which may be used in potential additional clinical trials together with RG-101 following completion of the planned Phase II study. Neither party has any further obligations or commitments beyond the contemplated study under the Clinical Trial Collaboration.

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, 2014 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, 2014, or Annual Report, filed with the Securities and Exchange Commission on February 19, 2015. 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, though not all

forward-looking statements necessarily contain these identifying words. Such statements may include, but are not limited to, statements concerning the following:

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- the initiation, cost, timing, progress and results of, and our expected ability to undertake certain activities and accomplish certain goals with respect to our research and development activities, preclinical studies and future clinical trials;
- our ability to obtain and maintain regulatory approval of our future product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our future product candidates;
- our strategic alliance partners' election to pursue development and commercialization of any programs or future product candidates that are subject to our collaboration and license agreements with such partners;
- our ability to attract collaborators with relevant 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, and our expectations regarding future therapeutic and commercial potential with respect to 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, if any;
- 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;
- the accuracy of our estimates regarding future expenses, future revenues, capital requirements and need for additional financing; and
- the additional risks and other factors described under the caption "Risk Factors" under Part II, 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 microRNAs to treat a broad range of diseases. We were formed in 2007 when Alnylam Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc. contributed significant intellectual property, know-how and financial and human capital to pursue the development of drugs targeting microRNAs pursuant to a license and collaboration agreement. We have established strategic alliances with AstraZeneca AB and Sanofi to discover, develop and commercialize microRNA therapeutics. Under these strategic alliances, we are eligible to receive approximately $900.0 million in aggregate milestone payments upon successful commercialization of microRNA therapeutics for the programs contemplated by our agreements. These payments include up to $107.8 million upon achievement of preclinical and investigational new drug, or IND, milestones, up to $138.0 million upon achievement of clinical development milestones, up to $180.0 million upon achievement of regulatory milestones and up to $490.0 million upon achievement of commercialization milestones.

microRNAs are 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 microRNAs is directly linked to many diseases. To date, approximately 800 microRNAs have been identified in humans, each of which is believed to interact with a specific set of genes that control key aspects of cell biology. Since most diseases are multi-factorial and involve multiple targets in a pathway, the ability to modulate gene networks by targeting a single microRNA provides a new therapeutic approach for treating complex diseases.

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RNA plays an essential role in the process used by cells to encode and translate genetic information from DNA to proteins. RNA is comprised of subunits called nucleotides and is synthesized from a DNA template by a process known as transcription. Transcription generates different types of RNA, including messenger RNAs that carry the information for proteins in the sequence of their nucleotides. In contrast, microRNAs are RNAs that do not code for proteins but rather are responsible for regulating gene expression by affecting the translation of target messenger RNAs. By interacting with many messenger RNAs, a single microRNA can regulate several genes that are instrumental for the normal function of a biological pathway.

We believe that microRNA therapeutics have the potential to become a new and major class of drugs with broad therapeutic application for the following reasons:

- microRNAs, until recently, have not been a focus of pharmaceutical research;
- microRNAs play a critical role in regulating biological pathways by controlling the translation of many target genes;
- microRNA therapeutics target entire disease pathways which may result in more effective treatment of complex multi-factorial diseases; and
- microRNA therapeutics may be synergistic with other therapies because of their different mechanism of action.

We believe we have assembled the leading position in the microRNA field, including expertise in microRNA biology and oligonucleotide chemistry, a broad intellectual property estate, relationships with key opinion leaders and a disciplined drug discovery and development process. We refer to these assets as our microRNA product platform. We are using our microRNA product platform to develop chemically modified, single-stranded oligonucleotides that we call anti-miRs to modulate microRNAs and return diseased cells to their healthy state. We believe microRNAs may be transformative in the field of drug discovery and that anti-miRs may become a new and major class of drugs with broad therapeutic application, much like small molecules, biologics and monoclonal antibodies. In addition to our microRNA product platform, we have established Regulus microMarkers[SM], a division focused on identifying microRNAs as biomarkers of human disease to support our therapeutic pipeline, collaborators and strategic partners. Regulus microMarkers[SM] utilizes a clinically-validated, highly reproducible technology platform to identify microRNAs as potential biomarkers for disease and we control key intellectual property and know-how related to the division. We believe that microRNA biomarkers may be used to select optimal patient segments in clinical trials and to monitor disease progression or relapse. We believe these microRNA biomarkers can be applied toward drugs that we develop and drugs developed by other companies with which we partner or collaborate. We have formed a research collaboration with Biogen focused on the discovery of microRNAs as biomarkers for multiple sclerosis and have also entered into an arrangement with another leading, commercial-stage pharmaceutical company to explore microRNAs as biomarkers for specific patient populations. We also maintain several academic research collaborations focused on the identification of microRNAs as biomarkers in multiple disease areas.

‘Clinical Map Initiative’ Goals

To advance our microRNA therapeutics pipeline and biomarkers platform over the next several years, we have outlined specific goals under our ‘Clinical Map Initiative’ strategy. We are developing RG-101 and RG-012, an anti-miR targeting microRNA-21 for the treatment of Alport syndrome, a life-threatening kidney disease driven by genetic mutations with no approved therapy. We are also advancing several programs toward clinical development in oncology, fibrosis and metabolic diseases, both independently and with our strategic alliance partners AstraZeneca and Sanofi. Under our strategic alliance with AstraZeneca, AstraZeneca recently selected RG-125, a GalNAc-conjugated anti-miR targeting microRNA-103/107 for the treatment of nonalcoholic steatohepatitis, or NASH, in patients with type 2 diabetes/pre-diabetes.

RG-101: In August 2015, we initiated a Phase II study investigating RG-101 in combination with oral direct-acting antiviral agents Harvoni®, Olysio®, and Daklinza® for 28 days. In early 2016, interim data is expected to be reported and sustained viral response data 12 weeks following conclusion of treatment (SVR12) is expected to be reported in the second quarter of 2016. To expand the potential development of RG-101, we recently entered into a clinical trial collaboration and formulation agreement with GSK LLC. In the first quarter of 2016, we plan to initiate a Phase II study evaluating the potential to achieve sustained viral responses post treatment with a single subcutaneous administration of RG-101 in combination with daily oral administrations of GSK2878175, a non-nucleoside NS5B

polymerase inhibitor, for up to 12 weeks in treatment-naïve patients chronically infected with HCV genotypes 1 and 3. Concurrently, GSK will work on developing a long-acting parenteral formulation for injection ("LAP") of GSK2878175 which could improve patient compliance through reduced dosing intervals and potentially extend opportunities for HCV therapeutic intervention. This LAP formulation of GSK2878175 may be used in potential additional clinical trials together with RG-101 following completion of the planned Phase II study. Neither us nor GSK has any further obligations or commitments beyond the contemplated study under the clinical trial collaboration agreement.

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RG-012: In June 2015, we initiated a Phase I study to evaluate the safety, tolerability and pharmacokinetics of subcutaneous dosing of RG-012 in healthy volunteers and the study is now complete. 40 healthy volunteer subjects were enrolled in this first-in-human, single ascending dose study. RG-012 was well-tolerated and there were no serious adverse events reported. We also continue to enroll Alport syndrome patients in our global ATHENA natural history of disease study, which is designed to characterize the natural decline of renal function (as measured by established renal markers) in Alport syndrome patients over time. We believe the data from the ATHENA study will provide the clinical basis for the design of a Phase II proof-of-concept study to monitor the therapeutic effect of RG-012 on the decline in renal function in patients with Alport syndrome. In the first half of 2016, we plan to initiate a Phase II proof-of-concept study evaluating the efficacy of RG-012 in Alport syndrome patients.

RG-125: AstraZeneca plans to initiate a Phase I study evaluating RG-125 in humans by the end of 2015.

FINANCIAL OPERATIONS OVERVIEW

Revenue

Our revenues generally consist of upfront payments for licenses or options to obtain licenses in the future, milestone payments and payments for other research services under strategic alliance and collaboration agreements.

In the future, we may generate revenue from a combination of license fees and other upfront payments, payments for research and development services, 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 microMarkers[SM] 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, other clinical trial related vendors, consultants and our scientific advisors;
-