Regulus Therapeutics Inc.
Form 10-Q
November 02, 2016
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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, 2016
or
¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE TRANSITION PERIOD FROM TO
Commission file number: 001-35670
Regulus Therapeutics Inc.
(Exact name of registrant as specified in its charter)

Delaware	26-4738379
(State or Other Jurisdiction of Incorporation or Organization)	(I.R.S. Employer Identification No.)
10614 Science Center Drive San Diego, CA	92121
(Address of Principal Executive Offices)	(Zip Code)

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨
Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨
Indicate by check mark whether registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer", "accelerated filer", and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ¨	Accelerated filer 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 28, 2016, the registrant had 52,923,305 shares of Common Stock ($0.001 par value) outstanding.

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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)

	September 30, 2016 (Unaudited)	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 14,706	$ 15,960
Short-term investments	76,877	98,103
Restricted cash	80	1,256
Prepaid expenses	10,614	8,159
Contract and other receivables	286	10,021
Other current assets	267	759
Total current assets	102,830	134,258
Property and equipment, net	12,042	5,400
Intangibles, net	1,051	1,081
Other assets	343	344
Total assets	$ 116,266	$ 141,083
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,724	$ 2,717
Accrued liabilities	5,066	6,329
Accrued compensation	2,290	2,392
Current portion of deferred revenue	72	1,194
Total current liabilities	13,152	12,632
Term loan, less debt issuance costs	19,787	—
Deferred revenue, less current portion	2,011	2,065
Other long-term liabilities	8,631	2,308
Total liabilities	43,581	17,005
Commitments and Contingencies		
Stockholders' equity:		
Common stock, $0.001 par value; 200,000,000 shares authorized, 52,923,305 and 52,669,266 shares issued and outstanding at September 30, 2016 (unaudited) and December 31, 2015, respectively	53	53
Additional paid-in capital	326,076	315,673
Accumulated other comprehensive loss	(113)	(133)
Accumulated deficit	(253,331)	(191,515)
Total stockholders' equity	72,685	124,078
Total liabilities and stockholders' equity	$ 116,266	$ 141,083

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,	
	2016	2015	2016	2015
	(Unaudited)			
Revenues:				
Revenue under strategic alliances and collaborations	$204	$1,865	$1,176	$9,899
Total revenues	204	1,865	1,176	9,899
Operating expenses:				
Research and development	14,554	10,965	49,326	43,593
General and administrative	4,842	4,245	13,609	13,703
Total operating expenses	19,396	15,210	62,935	57,296
Loss from operations	(19,192)	(13,345)	(61,759)	(47,397)
Other income (expense):				
Interest and other income	237	335	608	686
Interest and other expense	(560)	(6)	(674)	(22)
Loss from valuation of convertible note payable	—	—	—	(1,811)
Loss before income taxes	(19,515)	(13,016)	(61,825)	(48,544)
Income tax (expense) benefit	(4)	16	9	22
Net loss	$(19,519)	$(13,000)	$(61,816)	$(48,522)
Other comprehensive loss:				
Unrealized (loss) gain on short-term investments, net	(30)	40	20	96
Comprehensive loss	$(19,549)	$(12,960)	$(61,796)	$(48,426)
Net loss per share, basic and diluted	$(0.37)	$(0.25)	$(1.17)	$(0.95)
Weighted average shares used to compute basic and diluted net loss per share	52,835,414	51,990,460	52,776,459	51,052,068

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,	
	2016	2015
	(Unaudited)	
Operating activities		
Net loss	$(61,816)	$(48,522)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization expense	1,589	1,177
Loss from valuation of convertible note payable	—	1,811
Stock-based compensation	9,453	11,607
Amortization of premium on investments, net	525	1,130
Other	338	73
Change in operating assets and liabilities:		
Contracts and other receivables	9,735	(50)
Prepaid expenses	(2,455)	(116)
Other assets	492	25
Accounts payable	3,007	1,024
Accrued liabilities	(1,187)	1,649
Accrued compensation	(102)	(109)
Deferred revenue	(1,176)	(2,257)
Deferred rent and other liabilities	(178)	(257)
Net cash used in operating activities	(41,775)	(32,815)
Investing activities		
Purchases of short-term investments	(60,716)	(67,064)
Sales and maturities of short-term investments	81,437	76,411
Purchases of property and equipment	(746)	(873)
Acquisition of intangibles	(48)	(40)
Net cash provided by investing activities	19,927	8,434
Financing activities		
Proceeds from borrowing under term loan, net	19,768	—
Proceeds from issuance of common stock, net	641	492
Proceeds from exercise of common stock options	309	5,001
Principal payments on other long-term obligations	(124)	(115)
Net cash provided by financing activities	20,594	5,378
Net decrease in cash and cash equivalents	(1,254)	(19,003)
Cash and cash equivalents at beginning of period	15,960	37,327
Cash and cash equivalents at end of period	$14,706	$18,324
Supplemental disclosure of cash flow information		
Net changes in restricted cash	$(1,176)	$1,400
Interest paid	$(518)	$(22)
Income taxes paid	$(1)	$(1)
Supplemental disclosure of non-cash investing and financing activities		
Allowance for tenant improvements	$6,653	$—
Amounts accrued for property and equipment	$14	$179
Amounts accrued for patent expenditures	$5	$—

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 audited financial statements and footnotes included in our Annual Report on Form 10-K for the year ended December 31, 2015, 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"), 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, which approximates effort over our estimated period of performance, which for us is typically 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 acknowledgment 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.

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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 estimated 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. The balance of our convertible note payable, which was valued under the fair value option, was converted into shares of common stock in January 2015 (see Note 4).

Clinical Trial and Preclinical Study Accruals

We make estimates of our accrued expenses for clinical trial and preclinical study activities as of each balance sheet date in our financial statements based on the facts and circumstances known to us at that time. These accruals are based upon 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 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. As of September 30, 2016, our restricted cash balance was $0.1 million.

Prepaid Materials

We capitalize the purchase of certain raw materials and related supplies for use in the manufacturing of drug product in our clinical development programs, as we have determined that these materials have alternative future use. We can use these raw materials and related supplies in multiple clinical drug products, and therefore have future use

independent of the development status of any particular drug program until it is utilized in the manufacturing process. We periodically review these capitalized materials for indicators of impairment, including shelf life, continued alternative future use and obsolescence.

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We have not recorded any adjustments to the carrying value of these materials to date. As of September 30, 2016 and December 31, 2015, our prepaid materials balance was $6.9 million and $5.5 million, respectively, which amounts are included in prepaid expenses in our consolidated balance sheets.

Recent Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-09, Revenue from Contracts with Customers. Adoption of ASU No. 2014-09 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 statements.

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 statements.

In April 2015, the FASB issued ASU No. 2015-03, Interest- Imputation of Interest: Simplifying the Presentation of Debt Issuance Costs, which requires that debt issuance costs related to a recognized debt liability be presented in the balance sheet as a direct deduction from the carrying amount of that debt liability, consistent with debt discounts. The recognition and measurement guidance for debt issuance costs were not affected by the amendments in ASU No. 2015-03. In June 2016, upon entering into a loan and security agreement, we adopted ASU No. 2015-03, which resulted in the classification of $0.2 million of debt issuance costs against the principal balance of our outstanding term loan of $20.0 million.

In January 2016, the FASB issued ASU No. 2016-01, Recognition and Measurement of Financial Assets and Financial Liabilities, which eliminates the requirement for public companies to disclose the method(s) and significant assumptions used to estimate the fair value that is required to be disclosed for financial instruments measured at amortized cost on the balance sheet. Additionally, the standard requires public companies to use the exit price notion when measuring the fair value of financial instruments for disclosure purposes. Furthermore, the standard requires presentation of financial assets and liabilities by measurement category and form of financial asset on the balance sheet or accompanying notes to the financial statements. The standard is effective for annual reporting periods beginning after December 15, 2017, including interim periods within those annual reporting periods. Early application is permitted. We are currently evaluating the impact of adoption on our financial statements.

In February 2016, the FASB issued ASU No. 2016-02, Leases, which increases transparency and comparability among organizations by requiring recognition of lease assets and lease liabilities on the balance sheet and disclosure of key information about leasing arrangements. The standard is effective for annual reporting periods beginning after December 15, 2018, including interim periods within those annual reporting periods. Early application is permitted. We are currently evaluating the impact of adoption on our financial statements.

In March 2016, the FASB issued ASU No. 2016-09, Compensation – Stock Compensation: Improvements to Employee Share-Based Payment Accounting, which is intended to simplify several aspects of accounting for share-based payment transactions, including the income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. The standard is effective for annual reporting periods beginning after December 15, 2016, and interim periods within those annual reporting periods. Early application is permitted. We are currently evaluating the impact of adoption on our financial statements.

In August 2016, the FASB issued ASU No. 2016-15, Statement of Cash Flows: Classification of Certain Cash Receipts and Cash Payments, which addresses the presentation and classification of certain cash receipts and cash payments in the statement of cash flows under Accounting Standards Codification 230. The standard is effective for annual reporting periods beginning after December 15, 2017, and interim periods within those fiscal years. Early application is permitted. The adoption of this guidance will have no impact on our financial statements.

2. Net Loss Per Share

Basic net loss per share is calculated by dividing 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 net loss

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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. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted net loss per share.

Potentially dilutive securities not included in the calculation of diluted net loss per share because to do so would be anti-dilutive consisted of 3,131,911 and 3,762,952 shares attributable to common stock options for the three and nine months ended September 30, 2016, respectively, compared to 2,269,605 and 2,499,389 shares attributable to common stock options for the same periods in 2015.

3. Investments

We invest our excess cash in commercial paper and debt instruments of financial institutions and corporations. As of September 30, 2016, 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	Unrealized Losses	Estimated fair value
As of September 30, 2016					
Corporate debt securities	2 or less	$ 66,294	$ 14	$ (63)	$ 66,245
Certificates of deposit	2 or less	7,640	—	—	7,640
Commercial paper	1 or less	2,993	—	(1)	2,992
Total		$ 76,927	$ 14	$ (64)	$ 76,877

	Maturity (in years)	Amortized cost	Unrealized Gains	Unrealized Losses	Estimated fair value
As of December 31, 2015					
Corporate debt securities	2 or less	$ 81,054	$ 16	$ (103)	$ 80,967
Certificates of deposit	2 or less	13,640	—	—	13,640
Commercial paper	1 or less	3,490	6	—	3,496
Total		$ 98,184	$ 22	$ (103)	$ 98,103

4. Fair Value Measurements

We have certain financial assets 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 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.

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- 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.

Financial Assets Measured at Fair Value

The following table presents our fair value hierarchy for assets measured at fair value on a recurring basis as of September 30, 2016 and December 31, 2015 (in thousands):

	Fair value as of September 30, 2016			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$12,802	$12,802	$—	$ —
Corporate debt securities	66,245	—	66,245	—
Certificates of deposit	7,640	—	7,640	—
Commercial paper	2,992	—	2,992	—
	$89,679	$12,802	$76,877	$ —

	Fair value as of December 31, 2015			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$15,152	$15,152	$—	$ —
Corporate debt securities	80,967	—	80,967	—
Certificates of deposit	13,640	—	13,640	—
Commercial paper	3,496	—	3,496	—
	$113,255	$15,152	$98,103	$ —

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.

Financial Liabilities Measured at Fair Value

In October 2012, in conjunction with our initial public offering, an amended and restated convertible promissory note originally issued to Glaxo Group Limited in February 2010 rolled over into a new promissory note (the "Post-IPO GSK Note"). The Post-IPO GSK Note was established in the principal amount of $5.4 million, with a maturity date of October 9, 2015. We used an income approach in the form of a convertible bond valuation model to value our convertible note payable. The convertible bond model considered the debt and option characteristics of the note.

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. A final valuation upon conversion 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 $1.8 million in the condensed statements of operations and comprehensive loss upon conversion in January 2015.

5. Term Loan

On June 17, 2016, we entered into a loan and security agreement ("Loan Agreement") with Oxford Finance, LLC, ("Oxford"), pursuant to which Oxford agreed to lend us up to $30.0 million, issuable in two separate term loans of $20.0 million (the "Term A Loan") and $10.0 million (the "Term B Loan"). We collectively refer to the Term A Loan and the Term B Loan as Term Loans. On June 22, 2016, we received $20.0 million in proceeds from the Term A Loan, net of debt issuance costs. Under the terms of the Loan Agreement we may, at our sole discretion, borrow $10.0 million under the Term B Loan following the achievement of a defined milestone event until the earlier of 60 days

thereafter or March 31, 2017.

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All outstanding Term Loans will mature on June 1, 2020 (the "Maturity Date") and we will have interest-only payments through June 1, 2018, followed by 24 equal monthly payments of principal and unpaid accrued interest. The Term Loans will bear interest at a floating per annum rate equal to (i) 8.51% plus (ii) the greater of (a) the 30 day U.S. Dollar LIBOR rate reported in The Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue and (b) 0.44%.

We have the option to prepay all, but not less than all, of the borrowed amounts, provided that we will be obligated to pay a prepayment fee equal to (i) 2% of the outstanding principal balance of the applicable Term Loan if prepayment is made prior to the second anniversary of the applicable funding date of the Term Loan, provided no prepayment fee will be due in connection with a prepayment made on or prior to the first anniversary of the applicable funding date of the Term Loan in connection with an acquisition of our company, or (ii) 1% of the applicable Term Loan prepaid thereafter and prior to the Maturity Date. We will be required to make a final payment of 5.5% of the principal balance outstanding, payable on the earlier of (i) the Maturity Date, (ii) acceleration of any Term Loan, or (iii) the prepayment of the Term Loans.

We may use the proceeds from the Term Loans solely for working capital and to fund our general business requirements. Our obligations under the Loan Agreement are secured by a first priority security interest in substantially all of our current and future assets, other than our intellectual property. We have also agreed not to encumber our intellectual property assets, except as permitted by the Loan Agreement.
As of September 30, 2016, we had $20.0 million outstanding under the Term A Loan. The Term A Loan was recorded at its initial carrying value of $20.0 million, less debt issuance costs of approximately $0.2 million. In connection with the Term A Loan, the debt issuance costs have been recorded as a debt discount in our consolidated balance sheets, which are being recorded as interest expense over the life of the Term A Loan using an effective interest rate of 8.98%. The exit fee is being accrued over the life of the Term A Loan through interest expense.
As of September 30, 2016, we were in compliance with all material covenants under the Loan Agreement.

Future principal payments for the Term A Loan due under the Loan Agreement are as follows (in thousands):

2016	$—
2017	—
2018	5,000
2019	10,000
2020	5,000
	$20,000

6. Stockholders' Equity
Shares Reserved for Future Issuance
The following shares of common stock were reserved for future issuance as of September 30, 2016:

Common stock options outstanding	6,621,106
Common stock available for future grant under 2012 Equity Incentive Plan	2,448,385
Common stock available for future grant under 2015 Inducement Plan	581,806
Employee Stock Purchase Plan	1,594,452
Total common shares reserved for future issuance	11,245,749

The following table summarizes our stock option activity under all equity incentive plans for the nine months ended September 30, 2016 (shares in thousands):

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	Number of options	Weighted average exercise price
Options outstanding at December 31, 2015	5,126	$ 8.91
Granted	2,414	$ 6.57
Exercised	(88)	$ 3.50
Canceled/forfeited/expired	(831)	$ 10.41
Options outstanding at September 30, 2016	6,621	$ 7.94

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 Employee Stock Purchase Plan during the periods presented:

	Three months ended September 30,		Nine months ended September 30,	
	2016	2015	2016	2015
Stock options				
Risk-free interest rate	1.5%	1.7%	1.4%	1.8%
Volatility	80.0%	78.9%	79.9%	78.8%
Dividend yield	—	—	—	—
Expected term (years)	5.7	6.1	5.9	6.1
Performance stock options				
Risk-free interest rate	—	1.6%	1.4%	1.8%
Volatility	—	79.3%	79.3%	76.7%
Dividend yield	—	—	—	—
Expected term (years)	0.0	6.1	6.0	6.0
Employee stock purchase plan shares				
Risk-free interest rate	0.5%	0.2%	0.5%	0.1%
Volatility	94.5%	77.1%	85.4%	75.6%
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,	
	2016	2015	2016	2015
Research and development	$1,199	$1,048	$3,931	$6,500
General and administrative	2,268	1,586	5,522	5,107
Total	$3,467	$2,634	$9,453	$11,607

7. Strategic Alliances and Collaborations

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

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	Three months ended September 30,		Nine months ended September 30,	
	2016	2015	2016	2015
AstraZeneca	$186	$1,380	$1,122	$8,028
Sanofi	18	18	54	54
Biogen	—	467	—	1,817
Total	$204	$1,865	$1,176	$9,899

AstraZeneca

In August 2012, we entered into a collaboration and license agreement with AstraZeneca. Under the terms of the agreement, we 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 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 were 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 investigational new drug application ("IND") or the end of the research term, which ended in August 2016.

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, did not have stand-alone value. As a result, we recognized revenue related to the upfront payment on a straight-line basis over the period of performance, which was four years based on the term of the research and development plan and ended in August 2016.

In connection with the collaboration and license agreement and concurrently with our initial public offering, we sold AstraZeneca 6,250,000 shares of our common stock in a private placement at a price per share of $4.00. Under the terms of the Common Stock Purchase Agreement ("CSPA"), 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. The CSPA and collaboration and license agreement 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 a discount for lack of marketability, $4.3 million was attributed to the collaboration and license agreement. We recognized the $4.3 million into revenue ratably over the period of performance of the research and development plan under the collaboration over four years, which ended in August 2016.

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. In December 2015, we earned a $10.0 million clinical milestone payment upon AstraZeneca's first patient dosing in a first-in-human Phase I clinical study of RG-125. If RG-125 is successfully developed and commercialized through pre-agreed sales targets, we could receive additional milestone payments of up to $160.0 million, including up to $32.5 million for clinical milestones, and up to $127.5 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 to high single digits, depending upon the volume of sales, which royalties may be reduced in certain, limited circumstances.

We evaluated the contingent event-based payments under our collaboration and license agreement with AstraZeneca and determined that the preclinical milestone and the milestone earned for the initiation of a Phase I clinical trial met the definition of substantive milestones. Accordingly, revenue for these achievements was recognized in its entirety in the period when the milestone was achieved and collectability was 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.

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 agreed to perform additional miR-103/107 program research and development activities related to RG-125. AstraZeneca 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 funded 100% of the costs for product manufacturing activities outlined in the letter agreement necessary to support a Phase I clinical study. In December 2015, we completed a technology transfer to AstraZeneca and have no further obligations to AstraZeneca for future development of RG-125. We recognized $0.9 million and $4.1 million for the three and nine months ended September 30, 2015, respectively,

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for the performance of research and development and product manufacturing activities outlined in the letter agreement. As of December 31, 2015, our obligations under the letter agreement were complete.

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.

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, 2016, 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 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 clinical 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. We are 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, 2016, deferred revenue associated with the Purchase Agreement and the 2014 Sanofi Amendment was $0.2 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

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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.

Biogen

In August 2014, we entered into a collaboration and license agreement with Biogen to collaborate on microRNA biomarkers for multiple sclerosis. Pursuant to the terms of the collaboration and license agreement, we received an upfront payment of $2.0 million, which was treated as a single unit of accounting as the license did not have stand-alone value. The $2.0 million up-front payment was recognized on a straight line basis over the estimated period of performance of approximately one year, ending September 2015.

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 December 31, 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 collaboration and license agreement of $0.1 million, $0.3 million and $0.3 million, respectively. These milestone payments met the definition of substantive milestones, and accordingly, revenue for these achievements was recognized in the period the milestones were achieved and collectability was reasonably assured.

8. Related Party Transactions

We have entered into certain 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 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 $0.2 million and $1.0 million for the three and nine months ended September 30, 2016, respectively, compared to zero and $0.4 million for the same periods in 2015.

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 Ionis Pharmaceuticals, Inc. 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, 2016.

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, 2015 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, 2015, or Annual Report, filed with the Securities and Exchange Commission on February 23, 2016. 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

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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:

- 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 clinical trials;
- our ability to obtain and maintain regulatory approval of our 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 product candidates;
- our strategic alliance partners' election to pursue development and commercialization of any programs or 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;
- future activities to be undertaken by our strategic alliance partners, collaborators and other third parties;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the size and growth potential of the markets for our 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 product candidates;
- the rate and degree of market acceptance of our 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;
- the accuracy of our estimates regarding future expenses, future revenues, capital requirements and need for additional financing; and
- the risks and other forward-looking statements 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 Ionis 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 $580 million in aggregate milestone payments upon successful commercialization of microRNA therapeutics and royalties on net sales for the programs contemplated by our agreements. These payments include up to $105.3 million upon achievement of preclinical and investigational new drug, or IND, milestones, up to $47.5 million

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upon achievement of clinical development milestones, up to $180.0 million upon achievement of regulatory milestones and up to $247.5 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 500 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.

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 completed a research collaboration with Biogen focused on the discovery of microRNAs as biomarkers for multiple sclerosis and have also completed research for 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.

Development Stage Pipeline

We currently have three programs in clinical development. Our most advanced program, RG-101, is a GalNAc-conjugated anti-miR targeting miR-122, a host factor for the hepatitis C virus, or HCV, infection. Our second program is RG-012, an anti-miR targeting microRNA-21 for the treatment of Alport syndrome, a life-threatening kidney disease driven by genetic mutations, currently with no approved therapy available. Our third program, under our strategic alliance with AstraZeneca is RG-125, a GalNAc-conjugated anti-miR targeting microRNA-103/107 for the treatment of nonalcoholic steatohepatitis, or NASH, in patients with Type II diabetes/pre-diabetes. AstraZeneca commenced clinical development of RG-125 in December 2015.

RG-101: We are currently evaluating RG-101 in several Phase I/II studies.

- In August 2015, we initiated a Phase II study investigating RG-101 designed to evaluate a shortened, four-week treatment regimen containing a subcutaneous administration of 2 mg/kg of RG-101 at Day 1 and Day 29, in

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combination with oral direct-acting antiviral agents Harvoni®, Olysio®, and Daklinza® for 28 days. In June 2016, we announced positive top-line results from the primary endpoint analysis of this clinical study:

Number and Percentage of Patients with Response at Various Timepoints

Time Since Treatment Completion	RG-101 + Harvoni®	RG-101 + Olysio®	RG-101 + Daklinza™
Week 12	27/27 (100%)	26/27 (96.3%)	22/24 (91.7%)*
Week 16	21/21 (100%)	19/20 (95.0%)	20/22 (90.9%)
Week 20	14/14 (100%)	13/15 (86.7%)	13/13 (100%)
Week 24	10/10 (100%)	8/10 (80.0%)	8/9 (88.9%)

*One patient missed the Week 12 visit. Viral load results for this patient at Week 8 and 16 were collected and indicate that the patient was a responder at both time points.

The results from this interim analysis demonstrated significant virologic response through 24 weeks of follow-up. RG-101 plus Harvoni continued to demonstrate 100% response rates. As previously reported, the combination of RG-101 plus either Olysio or Daklinza monotherapies have seen small numbers of viral relapse. The results reported include four new relapses: two in the Olysio arm (weeks 20 and 32) and two in the Daklinza arm (weeks 12 and 24). RG-101 in combination with four weeks of oral DAA therapy has been generally well tolerated with the majority of adverse events considered mild or moderate, and with no study discontinuations. Commonly reported adverse events, or AEs, included fatigue, headache, and injection site reactions. In addition, three out of 79 patients had experienced severe adverse events, or SAEs, as of the time of this analysis in June 2016.

- In November 2015, we entered into a clinical trial collaboration and formulation agreement with GSK LLC. In the first quarter of 2016, we initiated 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 initiated the development of a long-acting injectable formulation, or LAI, of GSK2878175, which could improve patient compliance through reduced dosing intervals and potentially extend opportunities for HCV therapeutic intervention.
- In May 2016, we expanded the clinical trial collaboration agreement with GSK to conduct a multi-centered, randomized, dose-ranging Phase II study evaluating the combination of RG-101 and GSK's LAI formulation of GSK2878175 as a potential single-visit cure in patients chronically infected with HCV. As with the initial collaboration, both parties will contribute to the costs associated with the study. Neither we nor GSK has any further obligations or commitments to each other beyond this expanded clinical collaboration agreement. This combination study has not yet been initiated.
- In January 2016, we initiated a multi-center, open label, non-randomized Phase I study to compare the safety, tolerability, pharmacokinetics, and pharmacodynamics of 2 mg/kg of RG-101 in subjects with severe renal insufficiency or end-stage renal disease (ESRD) to healthy control subjects, and further explore RG-101 in hepatitis C infected subjects with severe renal insufficiency or ESRD. The Phase I study has three treatment arms (n=24): (i) healthy volunteers (n=8); (ii) patients with severe renal impairment or ESRD (n=8); and (iii) HCV patients with severe renal impairment or ESRD (n=8). Enrollment was completed in the second quarter of 2016, and we anticipate reporting additional data from the HCV/severe renal impairment or ESRD arm before the end of 2016.

- In June 2016, we received verbal notice from the U.S. Food and Drug Administration, or FDA, that our IND for RG-101 for the treatment of chronic HCV infection has been placed on clinical hold. The FDA initiated the clinical hold after a second patient experienced an SAE of jaundice. This SAE occurred in an HCV patient with end-stage renal disease on dialysis enrolled in our on-going Phase I US study 117 days after receiving a single dose of RG-101. Timelines for our three on-going studies of RG-101 are not expected to be impacted as all patients have been enrolled and completed their dosing of RG-101 and will continue with protocol scheduled visits. In July 2016, we received a

formal clinical hold letter from the FDA requesting the following from us: detailed safety data analysis from preclinical and clinical studies; exploration of potential mechanisms of hepatoxicity in non-clinical models; review and input from independent hepatotoxicity experts; additional PK data from the US Phase I study; and a risk/benefit

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assessment for the proposed therapeutic regimen containing RG-101. Based upon the timing of our planned response to the FDA, we expect a response to our submission from the FDA in Q1 2017. We plan to work diligently with the FDA to seek the release of the clinical hold. Initiation of new RG-101 clinical studies are suspended pending resolution of the FDA clinical hold.

RG-012: In 2015, we completed a Phase I study to evaluate the safety, tolerability and pharmacokinetics of subcutaneous dosing of RG-012 in healthy volunteers. Forty 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. The data from the ATHENA study provided 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 September, we initiated the HERA study, an international randomized, double-blind, placebo-controlled, multi-center Phase II clinical trial designed to evaluate the safety, pharmacodynamics, pharmacokinetics, dose selection, and preliminary efficacy of weekly RG-012 injections in approximately 30 patients with Alport syndome. In order to address study design comments from European regulators, a multiple-ascending dose (MAD) study in healthy volunteers will be implemented (4-week repeat dosing) prior to expanding to Alport patients. We anticipate the MAD study will be completed in the first half of 2017. Based on predicted enrollment rates, we anticipate interim results from HERA in the first half of 2018.

RG-125: AstraZeneca initiated a Phase I study evaluating RG-125(AZD4076) in healthy volunteers in December 2015, earning us a $10.0 million milestone from the collaboration. In Q3 2016, AstraZeneca initiated a Phase I/IIa, randomized, single-blind, placebo-controlled, multiple ascending dose study in subjects with Type II diabetes and non-alcoholic fatty liver disease (NAFLD). AstraZeneca is responsible for all future development for RG-125.

We are advancing our preclinical portfolio towards clinical development in renal, hepatic, and central nervous system diseases both independently and with our strategic alliance partners Sanofi and AstraZeneca, and anticipate nominating a new clinical candidate by the end of 2016.

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;
- license fees; and

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- 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. Certain of the raw materials used in the process of manufacturing drug product are capitalized upon their acquisition and expensed upon usage, as we have determined these materials have alternative future use.

To date, we have conducted research on many different microRNAs 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 known targets based on our ongoing research. As a result, in the early phase of our development programs, 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 76 and have spent a total of approximately $243.5 million in research and development expenses through September 30, 2016.

We expect our research and development expenses to increase for the foreseeable future as we continue to conduct our ongoing clinical studies, initiate additional clinical studies and advance our preclinical research programs toward the clinic, including other IND-enabling activities. The process of conducting clinical trials and preclinical studies 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 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. 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.

Successful development of future product candidates 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 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 costs will likely include legal fees, Sarbanes-Oxley compliance and other accounting fees and directors’ and officers’ liability insurance premiums.

Other income (expense), net

Other income (expense) consists primarily of interest income and expense and various income or expense items of a non-recurring nature. We earn interest income from interest-bearing accounts and money market funds for cash and cash equivalents and marketable securities, such as interest-bearing bonds, for our short-term investments. Commencing in June 2016, interest expense is primarily attributable to interest charges associated with borrowings

under our term loan. We recorded periodic gains and losses from changes in value of a convertible note payable until its conversion into common stock in January 2015.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

There have been no significant changes to our critical accounting policies since December 31, 2015. For a description of critical accounting policies that affect our significant judgments and estimates used in the preparation of our consolidated financial statements, refer to Item 7 in Management's Discussion and Analysis of Financial Condition and Results of

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Operations and Note 1 to our financial statements contained in our Annual Report and Note 1 to our condensed financial statements contained in this quarterly report on Form 10-Q.

RESULTS OF OPERATIONS

Comparison of the three and nine months ended September 30, 2016 and 2015

The following table summarizes our results of operations for the three and nine months ended September 30, 2016 and 2015 (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2016	2015	2016	2015
Revenue under strategic alliances and collaborations	$204	$1,865	$1,176	$9,899
Research and development expenses	14,554	10,965	49,326	43,593
General and administrative expenses	4,842	4,245	13,609	13,703
Loss from valuation of convertible note payable	—	—	—	(1,811)

Revenue under strategic alliances and collaborations

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, milestone payments and payments for other research services. The following table summarizes our total revenues for the periods indicated (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2016	2015	2016	2015
AstraZeneca	$186	$1,380	$1,122	$8,028
Sanofi	18	18	54	54
Biogen	—	467	—	1,817
Total revenues under strategic alliances and collaborations	$204	$1,865	$1,176	$9,899

Revenue under strategic alliances was $0.2 million and $1.2 million for the three and nine months ended September 30, 2016, respectively, compared to $1.9 million and $9.9 million for the three and nine months ended September 30, 2015, respectively.

Revenue under the AstraZeneca collaboration and license agreement decreased to $0.2 million and $1.1 million for the three and nine months ended September 30, 2016, respectively, compared to $1.4 million and $8.0 million for the same periods in 2015. Revenue recognized in the three and nine months ended September 30, 2016 related to the amortization of upfront payments over the period of performance, which ended in August 2016. Revenue of $0.9 million and $4.1 million was recognized under the January 2015 letter agreement for the three and nine months ended September 30, 2015, respectively. As of December 31, 2015, our obligations under the letter agreement were complete. In March 2015, we earned a $2.5 million preclinical milestone payment for the clinical candidate selection of RG-125, a GalNAc-conjugated anti-miR targeting microRNA-103/107 for the treatment of NASH in patients with type II diabetes/pre-diabetes.

Revenue recognized from our collaboration and license agreement with Biogen decreased to zero for the three and nine months ended September 30, 2016, compared to $0.5 million and $1.8 million for the same periods in 2015, as a result of the completion of our performance under the collaboration and license agreement as of September 2015.

As of September 30, 2016, we had $2.1 million of deferred revenue, which consisted of payments received through our strategic alliances that have not yet been recognized in accordance with our revenue recognition policies.

Research and development expenses

Research and development expenses were $14.6 million and $49.3 million for the three and nine months ended September 30, 2016, respectively, compared to $11.0 million and $43.6 million for the three and nine months ended

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September 30, 2015, respectively. Personnel costs, including stock based compensation, increased by $1.0 million and general laboratory supply costs increased by $1.2 million for the three months ended September 30, 2016, compared to the same period in 2015, due to an increase in research personnel. Additionally, external services increased by $0.3 million for the three months ended September 30, 2016, compared to the same period in 2015, due to costs incurred associated with advancing our therapeutic pipeline.

Our aggregate preclinical and clinical trial costs increased by $0.5 million and $5.4 million for the three and nine months ended September 30, 2016, respectively, compared to the same periods in 2015. Clinical trial costs for RG-101 increased by $1.6 million and $8.2 million for the three and nine months ended September 30, 2016, respectively, compared to the same periods in 2015. These increases were due to incremental costs incurred associated with the initiation of a Phase II study for RG-101 in the first half of 2016. Program costs for RG-012 increased by $0.1 million and $2.6 million for the three and nine months ended September 30, 2016, respectively, compared to the same periods in 2015. These increases were due to increased costs associated with our global ATHENA natural history of disease study, increased drug product manufacturing costs and start-up costs for our Phase II study. These increases were partially offset by a decrease in preclinical study costs for RG-125 of $1.2 million and $5.4 million for the three and nine months ended September 30, 2016, respectively, compared to the same periods in 2015. In December 2015, AstraZeneca initiated a first-in-human Phase I clinical study of RG-125 and is responsible for all future costs associated with the development of RG-125.

We expect our research and development expenses to increase for the foreseeable future as we continue to conduct our ongoing clinical studies, initiate additional clinical studies and advance our preclinical research programs toward the clinic, including other IND-enabling activities.

General and administrative expenses

General and administrative expenses were $4.8 million and $13.6 million for the three and nine months ended September 30, 2016, respectively, compared to $4.2 million and $13.7 million for the three and nine months ended September 30, 2015, respectively. The increase of $0.6 million for the three months ended September 30, 2016 compared to the same period in 2015 was principally driven by an increase in non-cash stock-based compensation of $0.7 million. We expect our general and administrative expenses to increase for the foreseeable future as we expand our operating activities and incur additional costs associated with being a publicly traded company.

Loss from valuation of convertible note payable

On January 29, 2015, the principal amount outstanding under a $5.4 million convertible note issued by us to Glaxo Group Limited was converted into 1,356,738 shares of our common stock at a conversion price of $4.00 per share. Upon conversion, we recorded a loss from the change in value of the convertible note payable of $1.8 million for the nine months ended September 30, 2015.

LIQUIDITY AND CAPITAL RESOURCES

Since our inception through September 30, 2016, we have received $85.1 million principally from upfront payments, research funding and preclinical milestones from our strategic alliances and collaborations, $257.1 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, $45.8 million in net proceeds from our public offering in July 2013 and $76.3 million in net proceeds from our public offering in November 2014) and $19.8 million in net proceeds from our June 2016 secured term loan.

As of September 30, 2016, we had $91.7 million in cash, cash equivalents and short-term investments, including $0.1 million in restricted cash. The following table shows a summary of our cash flows for the nine months ended September 30, 2016 and 2015 (in thousands):

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	Nine months ended September 30,	
	2016	2015
	(unaudited)	
Net cash (used in) provided by:		
Operating activities	$(41,775)	$(32,815)
Investing activities	19,927	8,434
Financing activities	20,594	5,378
Total	$(1,254)	$(19,003)

Operating activities

Net cash used in operating activities was $41.8 million for the nine months ended September 30, 2016, compared to $32.8 million for the nine months ended September 30, 2015. The increase in net cash used in operating activities was attributable to an increase in net loss of $13.3 million for the nine months ended September 30, 2016, compared to the same period in 2015, and a $3.9 million reduction in non-cash charges, including stock-based compensation and changes in the value of our convertible note payable.

The increase in net cash used in operating activities was partially offset by changes in working capital, which resulted in net cash provided by operating activities of $8.1 million for the nine months ended September 30, 2016, compared to net cash used in operating activities of $0.1 million for the nine months ended September 30, 2015. This change was principally due to the receipt of $10.0 million from AstraZeneca in February 2016 for a milestone achieved in December 2015.

Investing activities

Net cash provided by investing activities for the periods presented primarily related 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 our liquidity needs. Net cash provided by the net sales and maturities of short-term investments was $20.7 million for the nine months ended September 30, 2016, compared to $9.3 million for the nine months ended September 30, 2015.

Financing activities

Net cash provided by financing activities was $20.6 million for the nine months ended September 30, 2016, compared to $5.4 million for the nine months ended September 30, 2015. The increase in net cash provided by financing activities was attributable to receipt of proceeds from the $20.0 million Term A Loan. The increase in net cash provided by financing activities was partially offset by a decrease in proceeds from the exercise of common stock options of $4.7 million for the nine months ended September 30, 2016, compared to the same period in 2015.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

As of September 30, 2016, 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, other than the following:

On June 17, 2016, we entered into a loan and security agreement with Oxford Finance, LLC, or Oxford, pursuant to which Oxford agreed to lend us up to $30.0 million, issuable in two separate term loans of $20.0 million (the Term A Loan) and $10.0 million (the Term B Loan). We collectively refer to the Term A Loan and the Term B Loan as the Term Loans. On June 22, 2016, we received $20.0 million in proceeds from the Term A Loan, net of debt issuance costs.

The Term A Loan matures on June 1, 2020. Repayment of the Term A Loan will be interest-only through June 1, 2018, followed by principal and interest payments thereafter and through maturity. The Term A Loan bears interest at a floating per annum rate equal to (i) 8.51% plus (ii) the greater of (a) the 30 day U.S. Dollar LIBOR rate on the last business day of the month that immediately precedes the month in which the interest will accrue and (b) 0.44%.

Off-Balance Sheet Arrangements

As of September 30, 2016, we did not have any off-balance sheet arrangements.

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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.

We also have interest rate exposure as a result of our Term A Loan. As of September 30, 2016, the outstanding principal amount of the Term A Loan was $20.0 million. The Term A Loan bears interest at a floating per annum rate equal to (i) 8.51% plus (ii) the greater of (a) the 30 day U.S. Dollar LIBOR rate reported in The Wall Street Journal on the last business day of the month that immediately precedes the month in which the interest will accrue and (b) 0.44%. Changes in the U.S. Dollar LIBOR rate may therefore affect our interest expense associated with the Term A Loan.

If a 10% change in interest rates were to have occurred on September 30, 2016, this change would not have had a material effect on the fair value of our investment portfolio or our interest expense 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 principal 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 recognizes 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, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As of September 30, 2016, we carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and our principal financial and accounting 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 principal executive officer and our principal financial and accounting officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of September 30, 2016.

Changes in Internal Control Over Financial Reporting

An evaluation was also performed under the supervision and with the participation of our management, including our principal executive officer and our principal financial and accounting 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

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None.

ITEM 1A. RISK FACTORS

You should carefully consider the following risk factors, as well as the other information in this report, before deciding whether to purchase, hold or sell shares of our common stock. The occurrence of any of the following risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You should consider all the factors described when evaluating our business. The risk factors set forth below that are marked with an asterisk (*) did not appear as separate risk factors in, or 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 biopharmaceutical 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 microRNA product platform, undertaking basic research around microRNA targets and conducting preclinical and clinical studies for our initial programs. We have initiated clinical development of RG-101 and RG-012, and AstraZeneca has initiated clinical development of RG-125 under our strategic alliance, however, we have not yet 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 $19.5 million and $13.0 million for the three months ended September 30, 2016 and 2015, respectively, and $61.8 million and $48.5 million for the nine months ended September 30, 2016 and 2015, respectively. As of September 30, 2016, we had an accumulated deficit of $253.3 million.

We have devoted most of our financial resources to research and development, including our preclinical and clinical development activities. To date, we have financed our operations primarily through the sale of equity securities and convertible debt, through our secured term loan from Oxford and from revenue received from our strategic alliance partners. We have a strategic alliance 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 and with AstraZeneca to continue the clinical development of RG-125 for NASH. Under our agreement with Sanofi, Sanofi has an option to obtain exclusive worldwide licenses for the development, manufacture and commercialization of potential product candidates selected from our programs. If Sanofi exercises its option to obtain a license to develop, manufacture and commercialize any such product candidate, it will assume responsibility for funding and conducting further clinical development and commercialization activities for such product candidate. However, if Sanofi 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 candidate and may not have the resources to do so unless we are able to enter into another strategic alliance for such product candidate. 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 initiated clinical development of RG-101 and RG-012, and AstraZeneca has initiated clinical development of RG-125, however, it will be several years, if ever, before we or our strategic alliance partners 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 and clinical development of our product candidates, both independently and under our strategic alliance agreements; seek to identify additional microRNA targets and

product candidates; acquire or in-license other products and technologies; continue with clinical development of 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, regulatory, research and administrative personnel; and create

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additional infrastructure to support our operations as a publicly traded 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 microRNAs as therapeutic targets;
- completing our research and preclinical development of product candidates;
- initiating and completing clinical trials for product candidates;
- seeking and obtaining marketing approvals for product candidates that successfully complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties;
- launching and commercializing 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 product candidates that we independently develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product. 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 towards or through clinical trials. 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 microRNA 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 additional 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.

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

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- 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.

Payments under the instruments governing our indebtedness may reduce our working capital. In addition, a default under our loan and security agreement could cause a material adverse effect on our financial position.*

In June 2016, we entered into a loan and security agreement with Oxford. Under the terms of the loan agreement, Oxford initially provided us with a Term A Loan of $20.0 million, with an additional $10.0 million Term B Loan available to us upon the achievement of a milestone until the earlier of 60 days after the achievement of the milestone or March 31, 2017, subject to the non-occurrence of a prior event of default. Our obligations under the loan agreement are secured by a first priority security interest in substantially all of our current and future assets, other than our intellectual property. We have also agreed not to encumber our intellectual property assets, except as permitted by the loan agreement. All of the Term Loans mature on June 1, 2020 and will be interest-only through June 1, 2018, followed by 24 equal monthly payments of principal and unpaid accrued interest. Payments under the loan agreement could result in a significant reduction of our working capital.

The loan agreement requires us, and any debt arrangements we may enter into in the future may require us, to comply with various covenants that limit our ability to, among other things:

- dispose of assets;
- complete mergers or acquisitions;
- incur indebtedness;
- encumber assets;
- pay dividends or make other distributions to holders of our capital stock;
- make specified investments; and
- engage in transactions with our affiliates.

These restrictions could inhibit our ability to pursue our business strategies. If we default under our obligations under the loan agreement, the lender could proceed against the collateral granted to it to secure our indebtedness or declare all obligation under the loan agreement to be due and payable. In certain circumstances, procedures by the lenders could result in a loss by us of all of our equipment and inventory, which are included in the collateral granted to the lenders. If any indebtedness under the loan agreement were to be accelerated, there can be no assurance that our assets would be sufficient to repay in full that indebtedness. In addition, upon any distribution of assets pursuant to any liquidation, insolvency, dissolution, reorganization or similar proceeding, the holders of secured indebtedness will be entitled to receive payment in full from the proceeds of the collateral securing our secured indebtedness before the holders of other indebtedness or our common stock will be entitled to receive any distribution with respect thereto.

We may incur additional indebtedness in the future. The debt instruments governing such indebtedness may contain provisions that are as, or more, restrictive than the provisions governing our existing indebtedness under the loan agreement. If we are unable to repay, refinance or restructure our indebtedness when payment is due, the lenders could proceed against the collateral or force us into bankruptcy or liquidation.

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

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December 31st of the preceding 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. In addition, we may grant or provide for the grant of rights to purchase shares of our common stock pursuant to our 2012 Employee Stock Purchase Plan, or the ESPP. The number of shares of our common stock reserved for issuance under the ESPP will automatically increase on January 1 of each calendar year by the lessor of 1% of the total number of shares of our common stock outstanding on December 31st of the preceding calendar year and 500,000 shares, 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, may 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 and the ESPP each year.

In addition, we have adopted an Inducement Plan pursuant to which our management may grant stock options exercisable for up to an aggregate of 1,000,000 shares of our common stock to new employees as inducements material to such new employees entering into employment with us. The number of shares which may be granted under the Inducement Plan may be increased in the future by our board of directors. In the event we grant options pursuant to our Inducement Plan, our stockholders may experience additional dilution, which could cause our stock price to fall.

RISKS RELATED TO THE DISCOVERY AND DEVELOPMENT OF PRODUCT CANDIDATES

The FDA has placed a clinical hold on RG-101, our most advanced compound under development, after a second patient experienced a serious adverse event of jaundice in our on-going Phase I study for the treatment of chronic HCV infection. Our business may be adversely affected if the clinical hold cannot be favorably resolved in a timely manner or if such regulatory concerns lead to more burdensome preclinical or clinical studies that cause significant delays or expense in developing our product candidates.*

In June 2016, the FDA placed a clinical hold on our RG-101 clinical program after a second patient experienced an SAE of jaundice. This SAE occurred in a HCV patient with end-stage renal disease on dialysis enrolled in our on-going Phase I U.S. study 117 days after receiving a single dose of RG-101. In accordance with the clinical hold, the FDA provided that no new dosing with RG-101 could be initiated in the United States. In July 2016, we received a formal clinical hold letter from the FDA requesting the following from us: detailed safety data analysis from preclinical and clinical studies; exploration of potential mechanisms of hepatoxicity in non-clinical models; review and input from independent hepatotoxicity experts; additional PK data from the US Phase I study; and a risk/benefit assessment for the proposed therapeutic regimen containing RG-101. Based upon the timing of our planned response to the FDA, we expect a response to our submission from the FDA in Q1 2017. It is possible that as the ongoing trials conclude, additional safety issues may be observed.

We cannot be certain whether or when the FDA will lift the clinical hold and allow us to pursue further development of RG-101 in the United States. If the FDA does not lift the clinical hold, our development timelines and our business may be adversely affected and our stock price may further decline. Further, even if the FDA lifts the clinical hold, the FDA or other regulatory agencies may continue to express safety concerns after the hold is lifted, and future preclinical or clinical studies involving RG-101 or combination regimens that include RG-101 may be more burdensome or include additional preclinical or clinical endpoints that are difficult to meet. In such instances, our progress in the development of this program may be significantly slowed and the associated costs may be significantly increased, adversely affecting our business.

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 microRNA technology, and our future success depends on the successful development of this technology and products based on our microRNA product platform. Neither we nor any other company has received regulatory approval to market therapeutics targeting microRNAs. 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 microRNA 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 microRNA 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.

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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 microRNA 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 studies and clinical trials of our product candidates may not be successful. If we are unable to successfully complete preclinical studies 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 development of product candidates that target microRNAs. 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 product candidates.

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

- successful completion of preclinical studies and clinical trials;
- receipt of marketing approvals from applicable regulatory authorities;
- obtaining and maintaining patent and trade secret protection for future product candidates;
- establishing and maintaining manufacturing relationships with third parties or establishing our own manufacturing capability; and
- successfully commercializing our products, if and when approved, whether alone or in collaboration with others.

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

If clinical trials of our 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 product candidates.*

Before obtaining marketing approval from regulatory authorities for the sale of product candidates, we or our strategic alliance partners must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are 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:

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- delays in reaching an agreement with the FDA or other regulatory authorities on final trial design;
- imposition of a clinical hold 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;
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