Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-Q

(Mark One)

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

FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2017

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 ☒ 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 ☒ No ☐

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

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐ (Do not check if a smaller reporting company)	Smaller reporting company	☐
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

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

As of November 3, 2017, the registrant had 103,955,147 shares of Common Stock ($0.001 par value) outstanding.

Table of Contents

REGULUS THERAPEUTICS INC.
TABLE OF CONTENTS

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements 3
Condensed Balance Sheets as of September 30, 2017 (Unaudited) and December 31, 2016 3
Condensed Statements of Operations and Comprehensive Loss for the three and nine months ended September 30, 2017 and 2016 (Unaudited) 4
Condensed Statements of Cash Flows for the nine months ended September 30, 2017 and 2016 (Unaudited) 5
Notes to Condensed Financial Statements (Unaudited) 6
Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations 16
Item 3. Quantitative and Qualitative Disclosures about Market Risk 22
Item 4. Controls and Procedures 23

PART II. OTHER INFORMATION

Item 1. Legal Proceedings 23
Item 1A. Risk Factors 24
Item 2. Unregistered Sales of Equity Securities and Use of Proceeds 47
Item 3. Defaults Upon Senior Securities 47
Item 4. Mine Safety Disclosures 47
Item 5. Other Information 48
Item 6. Exhibits 49

PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

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

	September 30, 2017	December 31, 2016
	(Unaudited)	
Assets		
Current assets:		
Cash and cash equivalents	$ 20,222	$ 14,941
Short-term investments	51,148	61,170
Contract and other receivables	532	1,657
Prepaid materials, net	5,912	5,552
Prepaid expenses and other current assets	1,752	4,154
Total current assets	79,566	87,474
Property and equipment, net	10,172	11,830
Intangibles, net	802	1,015
Other assets	307	342
Total assets	$ 90,847	$ 100,661
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 5,229	$ 5,840
Accrued liabilities	4,770	5,577
Accrued compensation	1,687	2,318
Current portion of deferred revenue	72	72
Total current liabilities	11,758	13,807
Term loan, less debt issuance costs	19,845	19,802
Deferred revenue, less current portion	1,939	1,993
Deferred rent, less current portion	8,372	8,840
Other long-term liabilities	351	144
Total liabilities	42,265	44,586
Commitments and Contingencies		
Stockholders' equity:		
Common stock, $0.001 par value; 200,000,000 shares authorized, 103,955,147 and 52,924,805 shares issued and outstanding at September 30, 2017 (unaudited) and December 31, 2016, respectively	104	53
Additional paid-in capital	379,992	329,496
Accumulated other comprehensive loss	(104)	(123)
Accumulated deficit	(331,410)	(273,351)
Total stockholders' equity	48,582	56,075
Total liabilities and stockholders' equity	$ 90,847	$ 100,661

See accompanying notes to these condensed financial statements.

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,	
	2017	2016	2017	2016
	(Unaudited)			
Revenues:				
Revenue under strategic alliances and collaborations	$ 18	$ 204	$ 54	$ 1,176
Total revenues	18	204	54	1,176
Operating expenses:				
Research and development	12,697	14,554	42,727	49,326
General and administrative	2,736	4,842	13,752	13,609
Total operating expenses	15,433	19,396	56,479	62,935
Loss from operations	(15,415)	(19,192)	(56,425)	(61,759)
Other income (expense):				
Interest and other income	160	237	559	608
Interest and other expense	(580)	(560)	(1,730)	(674)
Loss before income taxes	(15,835)	(19,515)	(57,596)	(61,825)
Income tax benefit (expense)	7	(4)	139	9
Net loss	$ (15,828)	$ (19,519)	$ (57,457)	$ (61,816)
Other comprehensive loss:				
Unrealized (loss) gain on short-term investments, net	(16)	(30)	19	20
Comprehensive loss	$ (15,844)	$ (19,549)	$ (57,438)	$ (61,796)
Net loss per share, basic and diluted	$ (0.18)	$ (0.37)	$ (0.88)	$ (1.17)
Weighted average shares used to compute basic and diluted net loss per share	90,072,045	52,835,414	65,550,749	52,776,459

See accompanying notes to these condensed financial statements.

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

	Nine months ended September 30,	
	2017	2016
	(Unaudited)	
Operating activities		
Net loss	$ (57,457)	$ (61,816)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization expense	1,942	1,589
Stock-based compensation	6,531	9,453
Amortization of premium on investments, net	271	525
Other	206	338
Change in operating assets and liabilities:		
Contracts and other receivables	1,124	9,735
Prepaid materials	(360)	(1,329)
Prepaid expenses and other assets	2,405	(634)
Accounts payable	(579)	3,007
Accrued liabilities	(652)	(1,187)
Accrued compensation	(631)	(102)
Deferred revenue	(54)	(1,176)
Deferred rent and other liabilities	(418)	(178)
Net cash used in operating activities	(47,672)	(41,775)
Investing activities		
Purchases of short-term investments	(48,539)	(60,716)
Sales and maturities of short-term investments	58,310	81,437
Purchases of property and equipment	(217)	(746)
Acquisition of intangibles	(16)	(48)
Net cash provided by investing activities	9,538	19,927
Financing activities		
Proceeds from borrowing under term loan, net	—	19,768
Proceeds from issuance of common stock, net	43,411	641
Proceeds from exercise of common stock options	4	309
Principal payments on other long-term obligations	—	(124)
Net cash provided by financing activities	43,415	20,594
Net increase (decrease) in cash and cash equivalents	5,281	(1,254)
Cash and cash equivalents at beginning of period	14,941	15,960
Cash and cash equivalents at end of period	$ 20,222	$ 14,706
Supplemental disclosure of cash flow information		
Net changes in restricted cash	$ —	$ (1,176)
Interest paid	$ (1,444)	$ (518)
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
Amounts accrued for patent expenditures	$ —	$ 5

See accompanying notes to these condensed financial statements.

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, 2016, from which the balance sheet information herein was derived.

We have incurred losses in each year since our inception. We expect to continue to incur significant expenses and operating losses for the foreseeable future in connection with our research and preclinical and clinical development of our product candidates. In order to continue to fund our research and development activities, we will need to seek additional capital. This may occur through strategic alliance and licensing arrangements and/or future public or private debt or equity financings. Sufficient funding may not be available, or if available, may be on terms that significantly dilute or otherwise adversely affect the rights of existing stockholders. If adequate funds are not available in the future, we may need to delay, reduce the scope of or put on hold one or more or our clinical and/or preclinical programs while we seek strategic alternatives.

In May 2017, we implemented a corporate restructuring to streamline our operations, reduce our operating expenses, extend our cash runway and focus our resources on our most promising programs. In connection with the restructuring, we committed to a reduction in our total workforce by approximately 30% percent, to approximately 65 employees. We completed the workforce reduction in June 2017. We recorded charges of approximately $3.2 million for employee severance and other related termination benefits in the second quarter of 2017, including $1.3 million in net adjustments to non-cash stock-based compensation. All payments associated with the corporate restructuring were paid in full as of June 30, 2017.

As of September 30, 2017, we had cash, cash equivalents and short-term investments of $71.4 million under Financial Accounting Standards Board, or FASB, Accounting Standards Update, or ASU, 2014-15, *Presentation of Financial Statements - Going Concern*. We have evaluated and concluded that there are no conditions or events, considered individually or in the aggregate, that raise substantial doubt about our ability to continue as a going concern for a period of one year following the date that these financial statements are issued.

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 agreement with Sanofi, 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.

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.

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.

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 expense the cost of materials when used. We periodically review these capitalized materials for continued alternative future use and write down the asset to its net realizable value in the period in which it is identified. As of September 30, 2017 and December 31, 2016, our net prepaid materials balance was $5.9 million and $5.6 million, respectively.

Recent Accounting Pronouncements

In May 2014, the FASB issued ASU No. 2014-09, *Revenue from Contracts with Customers (Topic 606)*, which outlines a single comprehensive model for entities to use in accounting for revenue arising from contracts with customers and supersedes most current revenue recognition guidance, including industry-specific guidance. ASU 2014-09 outlines a five-step process for revenue recognition that focuses on transfer of control, as opposed to transfer of risk and rewards, and also requires enhanced disclosures regarding the nature, amount, timing and uncertainty of revenues and cash flows from contracts with customers. Major provisions include determining which goods and services are distinct and require separate accounting (performance obligations), how variable consideration (which may include change orders and claims) is recognized, whether revenue should be recognized at a point in time or over time and ensuring the time value of money is considered in the transaction price.

The FASB issued supplemental adoption guidance and clarification to ASU No. 2014-09 in March 2016, April 2016 and May 2016 within ASU No. 2016-08, *Revenue from Contracts with Customers: Principal vs. Agent Considerations*, ASU No. 2016-10, *Revenue from Contracts with Customers: Identifying Performance Obligations and Licensing* and ASU No. 2016-12, *Revenue from Contracts with Customers: Narrow-Scope Improvements and Practical Expedients*, respectively. ASU No. 2014-09 and the related supplemental ASUs are effective for fiscal years beginning after December 15, 2017 and interim periods therein. The ASU permits two methods of adoption: the full retrospective method or the modified retrospective method. We plan to apply the modified retrospective method upon adoption in the first quarter of 2018 and currently do not anticipate that the adoption of this ASU will have a material impact with regard to our current contracts.

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 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. The adoption of this guidance will have no impact 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 was intended to simplify various aspects of accounting for share-based payment transactions. The new guidance requires immediate recognition of all excess tax benefits and deficiencies in the income statement, requires classification of excess tax benefits as an operating activity as opposed to a financing activity in the statements of cash flows and allows the Company to make an accounting policy election to either estimate the number of awards expected to vest or account for forfeitures when they occur. The standard is effective for annual reporting periods beginning after December 15, 2016, and interim periods within those annual reporting periods. We applied this standard in the first quarter of 2017 using the modified retrospective method of adoption. In conjunction with this adoption, we made an accounting policy election to account for forfeitures as they occur.

Upon adoption, we reversed a deferred tax asset related to the balance of unrecognized excess tax benefits of $7.4 million, with an offsetting adjustment to the valuation allowance. Under the modified retrospective method of adoption, we recorded an adjustment of $0.6 million to accumulated deficit with a corresponding offset to additional paid-in capital.

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 annual reporting periods. The adoption of this guidance will have no impact on our financial statements.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows: Restricted Cash*, which requires restricted cash and restricted cash equivalents to be included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts shown on the statement of cash flows. The standard is effective for annual reporting periods beginning after December 15, 2017, and interim periods within those annual reporting periods. Early application is permitted. Upon its adoption in 2018, we will include $1.3 million of restricted cash in our disclosed balance of cash and cash equivalents at the beginning of the period for 2016. We do not expect any additional impact on our financial statements.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation - Stock Compensation: Scope of Modification Accounting*, which provides clarity and guidance around which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. The standard is effective for annual reporting periods beginning after December 15, 2017, and interim periods within those annual reporting periods. The adoption of this guidance will have no impact on our financial statements unless we have modification accounting in accordance with Topic 718.

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 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 1,281,022 and 2,531,362 shares attributable to common stock options for the three and nine months ended September 30, 2017, respectively, compared to 3,131,911 and 3,762,952 shares attributable to common stock options for the same periods in 2016.

3. 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. As of September 30, 2017, 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, 2017					
Corporate debt securities	1 or less	$ 38,736	$ 1	$ (30)	$ 38,707
Certificates of deposit	2 or less	6,450	—	—	6,450
U.S. Treasury securities	2 or less	4,502	—	(6)	4,496
Debt securities of U.S. government-sponsored agencies	1 or less	1,497	—	(2)	1,495
Total		$ 51,185	$ 1	$ (38)	$ 51,148

	Maturity (in years)	Amortized cost	Unrealized Gains	Unrealized Losses	Estimated fair value
As of December 31, 2016					
Corporate debt securities	2 or less	$ 49,185	$ 12	$ (77)	$ 49,120
Certificates of deposit	1 or less	9,291	—	—	9,291
Commercial paper	1 or less	1,247	—	—	1,247
U.S. Treasury securities	1 or less	1,001	—	(1)	1,000
Debt securities of U.S. government-sponsored agencies	1 or less	512	—	—	512
Total		$ 61,236	$ 12	$ (78)	$ 61,170

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.
- 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, 2017 and December 31, 2016 (in thousands):

	Fair value as of September 30, 2017			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$ 18,078	$ 18,078	$ —	$ —
Corporate debt securities	38,707	—	38,707	—
Certificates of deposit	6,450	—	6,450	—
U.S. treasury securities	4,496	—	4,496	—
Debt securities of U.S. government-sponsored agencies	1,495	—	1,495	—
	$ 69,226	$ 18,078	$ 51,148	$ —

	Fair value as of December 31, 2016			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$ 13,578	$ 13,578	$ —	$ —
Corporate debt securities	49,120	—	49,120	—
Certificates of deposit	9,291	—	9,291	—
Commercial paper	1,247	—	1,247	—
U.S. treasury securities	1,000	—	1,000	—
Debt securities of U.S. government-sponsored agencies	512	—	512	—
	$ 74,748	$ 13,578	$ 61,170	$ —

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.

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"). On June 22, 2016, we received $20.0 million in proceeds from the Term A Loan, net of debt issuance costs. The ability to borrow on the Term B Loan expired on March 31, 2017. We refer to all amounts outstanding under the Loan Agreement as the Term Loan.

The outstanding Term Loan 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 Loan 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 amount, provided that we will be obligated to pay a prepayment fee equal to (i) 2% of the outstanding principal balance of the Term Loan if prepayment is made prior to the second anniversary of the funding date of the Term Loan, or (ii) 1% of the 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 the Term Loan, or (iii) the prepayment of the Term Loan.

We may use the proceeds from the Term Loan 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. The Loan Agreement defines certain events of default, including instances of a material adverse change in our operations, that may require prepayment of the outstanding Term Loan. No such events have occurred or are anticipated as of September 30, 2017.

As of September 30, 2017, we had $20.0 million outstanding under the Term Loan. The Term 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 Loan, the debt issuance costs have been recorded as a debt discount in our consolidated balance sheets, which are being accreted to interest expense over the life of the Term Loan using an effective interest rate of 8.98%. The exit fee is being accrued over the life of the Term Loan through interest expense.

As of September 30, 2017, we were in compliance with all covenants under the Loan Agreement.

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

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, 2017:

Common stock options outstanding	10,483,174
Common stock available for future grant under 2012 Equity Incentive Plan	1,240,667
Common stock available for future grant under 2015 Inducement Plan	41,948
Employee Stock Purchase Plan	1,675,110
Total common shares reserved for future issuance	13,440,899

The following table summarizes our stock option activity under all equity incentive plans for the nine months ended September 30, 2017 (shares in thousands):

	Number of options		Weighted average exercise price
Options outstanding at December 31, 2016	8,931	$	6.70
Granted	4,523	$	1.41
Exercised	(11)	$	0.38
Canceled/forfeited/expired	(2,960)	$	6.03
Options outstanding at September 30, 2017	10,483	$	4.62

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,	
	2017	2016	2017	2016
Stock options				
Risk-free interest rate	1.9%	1.5%	2.0%	1.4%
Volatility	89.5%	80.0%	89.4%	79.9%
Dividend yield	—	—	—	—
Expected term (years)	6.1	5.7	6.1	5.9
Performance stock options				
Risk-free interest rate	—	—	2.1%	1.4%
Volatility	—	—	89.9%	79.3%
Dividend yield	—	—	—	—
Expected term (years)	0	0	5.6	6.0
Employee stock purchase plan shares				
Risk-free interest rate	1.0%	0.5%	0.8%	0.5%
Volatility	104.5%	94.5%	110.7%	85.4%
Dividend yield	—	—	—	—
Expected term (years)	0.5	0.5	0.5	0.5

The following table summarizes the allocation of our stock-based compensation expense for all stock awards during the periods presented, including the adjustments to stock-based compensation expense associated with our May 2017 corporate restructuring (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2017	2016	2017	2016
Research and development	$ 653	$ 1,199	$ 2,411	$ 3,931
Research and development-restructuring related adjustments	—	—	(1,399)	—
General and administrative	631	2,268	2,840	5,522
General and administrative-restructuring related adjustments	—	—	2,679	—
Total	$ 1,284	$ 3,467	$ 6,531	$ 9,453

In connection with our May 2017 corporate restructuring we recorded a reversal of stock-based compensation in research and development expenses of $1.4 million as a result of the cancellation of unvested stock options. Additionally, we recorded additional stock-based compensation in general and administrative expenses of $2.7 million as a result of termination provisions within certain employment agreements. These amounts were recorded in the second quarter of 2017.

Public Offering

In July 2017, we completed an underwritten public offering of 50,600,000 shares of common stock at an offering price of $0.91 per share. We received net proceeds from the offering of $43.0 million after deducting underwriting discounts, commissions and other offering expenses payable by us.

7. Strategic Alliances and Collaborations

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

	Three months ended September 30,		Nine months ended September 30,	
	2017	2016	2017	2016
Sanofi	$ 18	$ 18	$ 54	$ 54
AstraZeneca	—	186	—	1,122
Total	$ 18	$ 204	$ 54	$ 1,176

Sanofi

In July 2012, we amended and restated our collaboration and license agreement with Sanofi to expand the potential therapeutic applications of the *micro*RNA alliance targets to be developed under such agreement. We determined that the elements within the strategic alliance agreement with Sanofi should be treated as a single unit of accounting because the delivered elements did not have stand-alone value to Sanofi. The following elements were delivered as part of the strategic alliance with Sanofi: (1) a license for up to four *micro*RNA targets; and (2) a research license under our technology alliance.

In June 2013, the original research term expired, upon which we and Sanofi entered into an option agreement pursuant to which Sanofi was granted an exclusive right to negotiate the co-development and commercialization of certain of our unencumbered *micro*RNA programs and we were granted the exclusive right to negotiate with Sanofi for co-development and commercialization of certain miR-21 anti-miRs in oncology and Alport syndrome. In July 2013, we received an upfront payment of $2.5 million, of which $1.25 million is creditable against future amounts payable by Sanofi to us under any future co-development and commercialization agreement we enter pursuant to the option agreement. Revenue associated with the creditable portion of this option payment remained deferred as of September 30, 2017, 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 *micro*RNA therapeutics to focus on specific orphan disease and oncology targets. Under the terms of our renewed alliance, Sanofi will have opt-in rights to our 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 *micro*RNA therapeutic products commercialized by Sanofi and will have the right to co-promote these products.

In connection with the 2014 Sanofi Amendment, we entered into a Common Stock Purchase Agreement (the "Purchase Agreement"), pursuant to which we sold 1,303,780 shares of our common stock to 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, 2017, 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 two years.

We are eligible to receive milestone payments of up to $101.8 million for proof-of-concept option exercise fees (net of $1.25 million creditable, as noted above), $15.0 million for clinical milestones and up to $300.0 million for regulatory and commercial milestones. In addition, we are entitled to receive royalties based on a percentage of net sales of any products from the miR-21 and miR-221/222 programs which, in the case of sales in the United States, will be in the middle of the 10 to 20% range, and, in the case of sales outside of the United States, will range from the low end to the middle of the 10 to 20% range, depending upon the volume of sales. If we exercise our option to co-promote a product, we will continue to be eligible to

receive royalties on net sales of each product in the United States at the same rate, unless we elect to share a portion of Sanofi's profits from sales of such product in the United States in lieu of royalties.

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

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 *micro*RNA alliance targets primarily in the fields of cardiovascular diseases, metabolic diseases and oncology. Pursuant to the agreement, we granted AstraZeneca an exclusive, worldwide license to 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 expired 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 which expired 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, which expired in August 2016.

In March 2015, we earned a $2.5 million preclinical milestone and in December 2015, we earned a $10.0 million clinical milestone. We determined the milestones to be substantive and recognized revenue upon achievement of each milestone.

In June 2017, AstraZeneca delivered written notice of their election to terminate the collaboration and license agreement. Effective upon the termination of the agreement, AstraZeneca's rights with respect to RG-125(AZD4076) will revert back to us. In accordance with the Agreement, the termination will become effective in June 2018, 12 months following the date of delivery of the notice by AstraZeneca.

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 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 engaged Sanofi Deutschland to manufacture RG-012 drug product and perform stability studies on our behalf. Expenses incurred under the agreement for services performed or out-of-pocket expenses were less than $0.1 million for the three and nine months ended September 30, 2017, respectively, compared to $0.2 million and $1.0 million for the same periods in 2016.

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, 2017 and 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, 2016 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, 2016, or Annual Report, filed with the Securities and Exchange Commission on March 3, 2017. Past operating results are not necessarily indicative of results that may occur in future periods.

FORWARD-LOOKING STATEMENTS

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

- 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 may 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;
- the expected benefits to be achieved from our May 2017 restructuring, including with respect to the expected reduction in our operating expenses and the extension of our cash runway;

- 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 clinical-stage biopharmaceutical company focused on discovering and developing first-in-class drugs targeting *micro*RNAs to treat diseases with significant unmet medical need. We were formed in 2007 when Alnylam Pharmaceuticals, Inc., or Alnylam, and Ionis Pharmaceuticals, Inc., or Ionis, contributed significant intellectual property, know-how and financial and human capital to pursue the development of drugs targeting *micro*RNAs pursuant to a license and collaboration agreement. Our most advanced program, under our strategic alliance with Sanofi, is RG-012, an anti-miR targeting miR-21 for the treatment of Alport syndrome, a life-threatening kidney disease driven by genetic mutations, currently with no approved therapy available.

*micro*RNAs are naturally occurring ribonucleic acid, or RNA, molecules that play a critical role in regulating key biological pathways. Scientific research has shown that an imbalance, or dysregulation, of *micro*RNAs is directly linked to many diseases. Furthermore, many different infectious pathogens interact and bind to host microRNA to survive. To date, over 500 *micro*RNAs have been identified in humans, each of which can bind to multiple messenger RNAs that control key aspects of cell biology. Since many diseases are multi-factorial, involving multiple targets and pathways, the ability to modulate multiple pathways by targeting a single *micro*RNA 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, *micro*RNAs are RNAs that do not code for proteins but rather are responsible for regulating gene expression by modulating the translation and decay of target messenger RNAs. By interacting with many messenger RNAs, a single *micro*RNA can regulate the expression of multiple genes involved in the normal function of a biological pathway. Many pathogens, including viruses, bacteria and parasites, also use host *micro*RNAs to regulate the cellular environment for survival. In some instances, the host *micro*RNAs are essential for the replication and/or survival of the pathogen. For example, miR-122 is a *micro*RNA expressed in human hepatocytes and is a key factor for the replication of the hepatitis C virus, or HCV.

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

- *micro*RNAs play a critical role in regulating biological pathways by controlling the translation of many target genes;
- *micro*RNA therapeutics regulate disease pathways which may result in more effective treatment of complex multi-factorial diseases;
- many human pathogens, including viruses, bacteria and parasites, use *micro*RNAs (host and pathogen encoded) to enable their replication and suppression of host immune responses; and
- *micro*RNA therapeutics may be synergistic with other therapies because of their different mechanism of action.

We believe we have assembled the leading position in the *micro*RNA field, including expertise in *micro*RNA biology and oligonucleotide chemistry, a broad intellectual property estate, relationships with key opinion leaders and a disciplined drug discovery and development process. We are using our *micro*RNA expertise to develop chemically modified, single-stranded oligonucleotides that we call anti-miRs to modulate *micro*RNAs and address underlying disease. We believe *micro*RNAs may play a critical role in complex disease and that targeting them with anti-miRs may become a source of a new and major class of drugs with broad therapeutic application, much like small molecules, biologics and monoclonal antibodies.

We believe that *micro*RNA biomarkers may be used to select optimal patient segments in clinical trials and to monitor disease progression or relapse. We believe these *micro*RNA 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 Inc. focused on the discovery of *micro*RNAs as biomarkers for multiple sclerosis and have also completed research for another

leading, commercial-stage pharmaceutical company to explore *micro*RNAs as biomarkers for specific patient populations. We also maintain several academic research collaborations focused on the identification of *micro*RNAs as biomarkers in multiple disease areas.

Development Stage Pipeline

We currently have multiple programs in various stages of clinical and preclinical development.

RG-012: In 2015, we completed a Phase I study to evaluate the safety, tolerability, and pharmacokinetics, or PK, of subcutaneous dosing of RG-012 in healthy volunteers. Forty healthy volunteer subjects were enrolled in this first-in-human, single ascending dose study. In May 2017, we completed a Phase I multiple-ascending dose, or MAD, study in 24 healthy volunteers (six-week repeat dosing) to determine safety, tolerability and PK of RG-012 prior to chronic dosing in patients. In both Phase I studies, RG-012 was well-tolerated, and there were no serious adverse events, or SAEs, reported. In the third quarter of 2017, we initiated HERA, the Phase II randomized (1:1), double-blinded, placebo-controlled study evaluating the safety and efficacy of RG-012 in 40 Alport syndrome patients. In parallel, a renal biopsy study was also initiated in the third quarter of 2017 to evaluate RG-012 renal tissue PK, target engagement and downstream effects on genomic disease biomarkers. Data from the renal biopsy study is anticipated in the first quarter of 2018 and an interim analysis from HERA is anticipated to be performed in the third quarter of 2018. In connection with the initiation of HERA and the renal biopsy study, we will discontinue enrollment of additional Alport syndrome patients in our global ATHENA natural history of disease study.

RGLS4326: Recently, we filed an investigational new drug, or IND, package with the U.S. Food and Drug Administration, or FDA, for RGLS4326, targeting microRNA-17 (miR-17) for the treatment of autosomal dominant polycystic kidney disease, or ADPKD.

RG-101: In July 2017, we discontinued clinical development of RG-101 for the treatment of chronic HCV infection. Comprehensive preclinical investigation and detailed analysis of clinical data from the RG-101 program had identified the direct inhibition of a hepatocyte conjugated bilirubin transporter as the likely mechanism for the cases of hyperbilirubinemia in the RG-101 program. We believe that a combination of factors, including inhibition of conjugated bilirubin transport by RG-101, impaired baseline bilirubin transport in HCV patients and the preferential uptake of RG-101 by hepatocytes contributed to this mechanism. Additional patient-specific contributing factors cannot be excluded. Applying the learnings from the RG-101 program, alternative compounds targeting miR-122 have been identified that maintain potent HCV antiviral activity while lacking inhibition of the bilirubin transporter. We believe these compounds have the potential for rapid clinical proof-of-concept of a novel, markedly shortened treatment regimen for HCV and will be considered for further development.

RG-125(AZD4076): In June 2017, AstraZeneca delivered written notice of their election to terminate the collaboration and license agreement. Effective upon the termination of the agreement, AstraZeneca's rights with respect to RG-125(AZD4076) for the treatment of non-alcoholic steatohepatitis, or NASH, in Type 2 Diabetes/Pre-diabetes will revert to us. In accordance with the Agreement, the termination will become effective in June 2018, which is 12 months following the date of delivery of the notice by AstraZeneca.

Preclinical Pipeline

A major focus of our preclinical research is targeting dysregulated *micro*RNAs implicated in diseases of high unmet medical need where we know we can effectively deliver to the target tissue or organ, such as the liver and kidney. Multiple *micro*RNAs have been identified as being dysregulated in NASH and these are in the process of target validation including the evaluation of tool compounds in animal models of NASH. Profiling of primary tumor cells from glioblastoma multiforme, or GBM, a rapidly fatal form of brain cancer, has identified miR-10b as a *micro*RNA target with the potential to inhibit tumor growth. We are investigating local and systemic delivery of anti-miR-10b oligonucleotides in preclinical models to evaluate potential for advancing this program to clinical testing in GBM. We also have early discovery programs investigating additional *micro*RNA targets for infectious diseases and indications for which there is *micro*RNA dysregulation.

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 our existing strategic alliance with Sanofi or future strategic alliances for one or more of our programs we establish, if any. 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 any strategic alliance partner. If Sanofi does not elect or otherwise agree to fund development costs for our RG-012 program for the treatment of Alport syndrome pursuant to our strategic alliance agreement, or if we or any potential future strategic alliance partner 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 and the development of our therapeutic programs. 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
- 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 *micro*RNAs with the goal of understanding how they function and identifying those that might be targets for therapeutic modulation. At any given time we are working on multiple targets, primarily within our therapeutic areas of focus. Our organization is structured to allow the rapid deployment and shifting of resources to focus on the best 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 clinical development program, RG-012 for the treatment of Alport syndrome, and preclinical pipeline.

Since our conversion to a corporation in January 2009, we have grown from 15 research and development personnel to 48 and have spent a total of approximately $301.3 million in research and development expenses through September 30, 2017.

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 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. Interest expense is primarily attributable to interest charges associated with borrowings under our secured term loan from Oxford.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

There have been no significant changes to our critical accounting policies since December 31, 2016. 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 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, 2017 and 2016

The following table summarizes our results of operations for the three and nine months ended September 30, 2017 and 2016 (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2017	2016	2017	2016
Revenue under strategic alliances and collaborations	$ 18	$ 204	$ 54	$ 1,176
Research and development expenses	12,697	14,554	42,727	49,326
General and administrative expenses	2,736	4,842	13,752	13,609
Interest and other expenses, net	(420)	(323)	(1,171)	(66)

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,	
	2017	2016	2017	2016
Sanofi	$ 18	$ 18	$ 54	$ 54
AstraZeneca	—	186	—	1,122
Total revenues under strategic alliances and collaborations	$ 18	$ 204	$ 54	$ 1,176

Revenue under strategic alliances was less than $0.1 million and $0.1 million for the three and nine months ended September 30, 2017, respectively, compared to $0.2 million and $1.2 million for the three and nine months ended September 30, 2016, respectively. The reduction in revenue for the three and nine months ended September 30, 2017 compared to the three and nine months ended September 30, 2016 was the result of the expiration of the AstraZeneca research and development plan under the collaboration in August 2016.

As of September 30, 2017, we had $2.0 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

The following tables summarize the components of our research and development expenses for the periods indicated, together with year-over-year changes (dollars in thousands):

	Three months ended September 30, 2017	% of total	Three months ended September 30, 2016	% of total	Increase (decrease) $	Increase (decrease) %
Research and development						
Personnel and internal expenses	$ 4,530	36%	$ 6,469	44%	$ (1,939)	(30)%
Third-party and outsourced expenses	7,046	55%	6,331	44%	715	11 %
Non-cash stock-based compensation	653	5%	1,199	8%	(546)	(46)%
Depreciation	488	4%	555	4%	(67)	(12)%
Total research and development expenses	$ 12,717	100%	$ 14,554	100%	$ (1,837)	

	Nine months ended September 30, 2017	% of total	Nine months ended September 30, 2016	% of total	Increase (decrease) $	Increase (decrease) %
Research and development						
Personnel and internal expenses	$ 17,231	40%	$ 17,964	36%	$ (733)	(4)%
Third-party and outsourced expenses	22,873	54%	26,046	53%	(3,173)	(12)%
Non-cash stock-based compensation	1,012	2%	3,931	8%	(2,919)	(74)%
Depreciation	1,631	4%	1,385	3%	246	18 %
Total research and development expenses	$ 42,747	100%	$ 49,326	100%	$ (6,579)	

Research and development expenses were $12.7 million and $42.7 million for the three and nine months ended September 30, 2017, respectively, compared to $14.6 million and $49.3 million for the three and nine months ended

September 30, 2016, respectively. The aggregate decrease in research and development expenses for the three months ended September 30, 2017 compared to the three months ended September 30, 2016 was driven by a $1.9 million reduction in personnel and internal costs, primarily attributable to a reduction in costs subsequent to our May 2017 corporate restructuring. The aggregate decrease in research and development expenses for the nine months ended September 30, 2017 compared to the nine months ended September 30, 2016 was driven by a $3.2 million reduction in external development costs, primarily driven by the wind-down of clinical activities related to the RG-101 program subsequent to the FDA clinical hold. Additionally, non-cash stock-based compensation decreased by $2.9 million for the nine months ended September 30, 2017, compared to the nine months ended September 30, 2016. This decrease was driven by a $1.4 million reversal of stock-based compensation as a result of the cancellation of unvested stock options in connection with our May 2017 corporate restructuring, in addition to a reduction in grant date fair value, and resulting non-cash stock-based compensation expense, of stock options granted in 2017 versus the comparative period.

General and administrative expenses

General and administrative expenses were $2.7 million and $13.8 million for the three and nine months ended September 30, 2017, respectively, compared to $4.8 million and $13.6 million for the three and nine months ended September 30, 2016, respectively. The decrease of $2.1 million for the three months ended September 30, 2017 compared to the three months ended September 30, 2016 was primarily driven by a reduction in non-cash stock-based compensation of $1.6 million, attributable to a reduction in grant date fair value, and resulting non-cash stock-based compensation expense, of stock options granted in 2017 versus the comparative period.

Interest and other expenses, net

Net interest and other expenses were $0.4 million and $1.2 million for the three and nine months ended September 30, 2017, respectively, compared to $0.3 million and $0.1 million for the three and nine months ended September 30, 2016, respectively. The net increase for the nine months ended September 30, 2017 compared to the nine months ended September 30, 2016 was driven by interest charges associated with our outstanding $20.0 million secured term loan from Oxford, which we borrowed in June 2016.

LIQUIDITY AND CAPITAL RESOURCES

Since our inception through September 30, 2017, we have received $85.1 million principally from upfront payments, research funding and preclinical milestones from our strategic alliances and collaborations, $300.1 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, $76.3 million in net proceeds from our public offering in November 2014 and $43.0 million in net proceeds from our public offering in July 2017) and $19.8 million in net proceeds from our June 2016 secured term loan.

We have incurred losses in each year since our inception. We expect to continue to incur significant expenses and operating losses for the foreseeable future in connection with our research and preclinical and clinical development of our product candidates. In order to continue to fund our research and development activities, we will need to seek additional capital. This may occur through strategic alliance and licensing arrangements and/or future public or private debt or equity financings. Sufficient funding may not be available, or if available, may be on terms that significantly dilute or otherwise adversely affect the rights of existing stockholders. If adequate funds are not available in the future, we may need to delay, reduce the scope of or put on hold one or more or our clinical and/or preclinical programs while we seek strategic alternatives.

As of September 30, 2017, we had cash, cash equivalents and marketable securities of $71.4 million. In July 2017, we completed an underwritten public offering of our common stock and received net proceeds from the offering of approximately $43.0 million after deducting underwriting discounts, commissions and other offering expenses payable by us. We believe our cash, cash equivalents and short-term investments as of September 30, 2017 will be sufficient to fund our operations for at least the next 12 months. We have evaluated and concluded that there are no conditions or events, considered individually or in the aggregate, that raise substantial doubt about our ability to continue as a going concern for a period of one year following the date that these financial statements are issued.

The following table shows a summary of our cash flows for the nine months ended September 30, 2017 and 2016 (in thousands):

	Nine months ended September 30,	
	2017	2016
	(unaudited)	
Net cash (used in) provided by:		
Operating activities	$ (47,672)	$ (41,775)
Investing activities	9,538	19,927
Financing activities	43,415	20,594
Total	$ 5,281	$ (1,254)

Operating activities

Net cash used in operating activities was $47.7 million for the nine months ended September 30, 2017, compared to $41.8 million for the nine months ended September 30, 2016. The increase in net cash used in operating activities was primarily attributable to changes in working capital, resulting in net cash provided by operating activities of $0.9 million for the nine months ended September 30, 2017, compared to net cash provided by operating activities of $8.1 million for the nine months ended September 30, 2016. Changes in working capital for the nine months ended September 30, 2016 included the receipt of a $10.0 million milestone payment under our strategic alliance with AstraZeneca.

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 our operations. We invest cash in excess of our immediate operating requirements in a way that maturity is staggered and designed 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 $9.8 million for the nine months ended September 30, 2017, compared to $20.7 million for the nine months ended September 30, 2016.

Financing activities

Net cash provided by financing activities was $43.4 million for the nine months ended September 30, 2017, compared to $20.6 million for the nine months ended September 30, 2016. The increase in net cash provided by financing activities was primarily attributable to $43.0 million in net proceeds received from our public offering in July 2017. Net cash provided by financing activities for the nine months ending September 30, 2016 included $19.8 million in net proceeds received from borrowings under our secured term loan with Oxford in June 2016.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

As of September 30, 2017, there have been no material changes, outside of the ordinary course of business, in our outstanding contractual obligations from those disclosed within "Management's Discussion and Analysis of Financial Condition and Results of Operations", as contained in our Annual Report.

Off-Balance Sheet Arrangements

As of September 30, 2017, we did not have any off-balance sheet arrangements.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

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

Because of the short-term maturities of our cash equivalents and marketable securities, we do not believe that an increase in market rates would have any significant impact on the realized value of our marketable securities. If a 10% change in interest rates were to have occurred on September 30, 2017, this change would not have had a material effect on the fair value of our investment portfolio as of that date.

We also have interest rate exposure as a result of our outstanding $20.0 million secured term loan from Oxford. As of September 30, 2017, the outstanding principal amount of the term loan was $20.0 million. The term 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 loan.

If a 10% change in interest rates were to have occurred on September 30, 2017, this change would not have had a material effect on 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 our principal financial and accounting 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, 2017, 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, or the Exchange Act. 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, 2017.

Changes in Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Rule 13a-15(f) of the Exchange Act. 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

On January 31, 2017, a putative class action complaint was filed by Baran Polat in the United States District Court for the Southern District of California, or District Court, against us, Paul C. Grint (our former Chief Executive Officer), and Joseph P. Hagan (then our Chief Operating Officer and currently our President and Chief Executive Officer). The complaint includes claims asserted, on behalf of certain purchasers of our securities, under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended. In general, the complaint alleges that, between January 21, 2016, and June 27, 2016, the defendants violated the federal securities laws by making materially false and misleading statements regarding our business and the prospects for RG-101, thereby artificially inflating the price of our securities. The plaintiff seeks unspecified monetary damages and other relief. On February 10, 2017, a second putative class action complaint was filed by Li Jin in the District Court against the Company, Mr. Hagan, Dr. Grint, and Timothy Wright, the Company's Chief Research and Development Officer. The Complaint alleges claims similar to those asserted by Mr. Polat. The actions have been related. On February17, 2017, the District Court entered an order stating that defendants need not answer, or otherwise respond, until the District Court enters an order appointing, pursuant to the Private Securities Litigation Reform Act of 1995, lead plaintiff and lead counsel, and the parties then submit a schedule to the District Court for the filing of an amended or consolidated complaint and the timing of

defendants' answer or response. On April 3, 2017, two motions for consolidation of the two actions, appointment of lead plaintiff and approval of counsel were filed in the actions, or the Consolidation and Lead Plaintiff Motions. On October 26, 2017, the District Court entered an order consolidating the cases, appointing lead plaintiffs, and appointing lead counsel for lead plaintiffs. We intend to vigorously defend this matter.

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 acquiring and in-licensing intellectual property rights, developing our *micro*RNA product platform, undertaking basic research around *micro*RNA targets and conducting preclinical and clinical studies for our initial programs. 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 $15.8 million and $57.5 million for the three and nine months ended September 30, 2017, respectively, compared to $19.5 million and $61.8 million for the three and nine months ended September 30, 2016, respectively. As of September 30, 2017, we had an accumulated deficit of $331.4 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. In June 2017, AstraZeneca provided notice to us of its election to discontinue the clinical development of RG-125(AZD4076) for NASH and terminated our collaboration and license agreement. Under the agreement with AstraZeneca, the termination will become effective on June 9, 2018, at which time AstraZeneca's rights to RG-125(AZD4076) will revert to us. 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 filed an IND package with the FDA for RGLS4326. We have also initiated clinical development of RG-012, 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 *micro*RNA 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 additional infrastructure to support our operations and our product development and planned future commercialization efforts.

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

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

- identifying and validating new *micro*RNAs as therapeutic targets;
- completing our research and preclinical development of 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. We believe our existing capital resources will be sufficient to fund our planned operations and expenditures for at least the next 12 months. However, we cannot provide assurances that our plans will not change or that changed circumstances will not result in the depletion of our capital resources more rapidly than we currently anticipate.

As we move future 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-012, RGLS4326 and any other future product candidates, we may have adverse results requiring mitigation strategies that may cause us to consume additional capital. Additionally, our strategic alliance partners may not elect to pursue the development and commercialization of any of our *micro*RNA product candidates that are subject to their respective strategic alliance agreements with us. Any of these events may increase our development costs more than we expect. For example, AstraZeneca terminated its development of RG-125(AZD4076). Upon the effective date of termination, AstraZeneca's rights to the program will revert to us and we may decide to continue with its development but will then be responsible for any continuing costs of development. 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
- 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 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. The ability to borrow on the Term B Loan expired on March 31, 2017. 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. Amounts outstanding under the loan agreement 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.

RISKS RELATED TO THE DISCOVERY AND DEVELOPMENT OF PRODUCT CANDIDATES

Preclinical and clinical studies of our product candidates may not be successful. If we are unable to generate successful results from our preclinical and clinical studies of our product candidates, or experience significant delays in doing so, our business may 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 *micro*RNAs. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates.

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

- successfully designing preclinical studies which may be predictive of clinical outcomes;
- successful results from preclinical and clinical studies;
- 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.

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

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

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

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

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

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

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to

identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

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:

- 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;
- delays caused by patients dropping out of a trial due to protocol procedures or requirements, product side effects or disease progression;
- clinical sites dropping out of a trial to the detriment of enrollment;
- time required to add new clinical sites; or
- delays by our contract manufacturers to produce and deliver sufficient supply of clinical trial materials.

For example, in June 2016, the FDA placed a full clinical hold on our RG-101 clinical program after a second patient experienced an SAE of jaundice. In July 2016, we received a formal clinical hold letter from the FDA requesting additional studies, expert opinion and detailed safety data analysis. In December 2016, we submitted a complete response to the FDA's initial request for information, however, the FDA later informed us that the full clinical hold placed on our RG-101 clinical development program in June 2016 would remain in effect pending the FDA's review of all requested data. We thereafter decided to discontinue clinical development of RG-101 upon completion of the one remaining clinical study since our evaluation of the clinical data from RG-101 led to the identification of a bilirubin transport mechanism as the likely cause for the cases of SAEs of jaundice. As a result, our progress in the development of this program was significantly slowed and the associated costs increased, potentially adversely affecting our business and causing a drop in our stock price.

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

- be delayed in obtaining marketing approval for our future product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as originally intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;

- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

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

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

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

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

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

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

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

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

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

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

Even if we obtain regulatory approval in the United States, the FDA may still impose significant restrictions on the indicated uses or marketing of our product candidates, or impose ongoing requirements for potentially costly post-approval studies or post-market surveillance. The holder of an approved NDA is obligated to monitor and report AEs and any failure of a

product to meet the specifications in the NDA. The holder of an approved NDA must also submit new or supplemental applications and obtain FDA approval for certain changes to the approved product, product labeling or manufacturing process. Advertising and promotional materials must comply with FDA rules and are subject to FDA review, in addition to other potentially applicable federal and state laws.

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

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

- issue a warning letter asserting that we are in violation of the law;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve a pending NDA or supplements to an NDA submitted by us;
- seize product; or
- refuse to allow us to enter into supply contracts, including government contracts.

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

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

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

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

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

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

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

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

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

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

RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES

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

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

- an alliance partner may shift its priorities and resources away from our programs due to a change in business strategies, or a merger, acquisition, sale or downsizing of its company or business unit;
- an alliance partner may cease development in therapeutic areas which are the subject of our strategic alliances;
- an alliance partner may change the success criteria for a particular program or potential product candidate thereby delaying or ceasing development of such program or candidate;

- a significant delay in initiation of certain development activities by an alliance partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- an alliance partner could develop a product that competes, either directly or indirectly, with an alliance product;
- an alliance partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- an alliance partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- an alliance partner may exercise its rights under the agreement to terminate a strategic alliance;
- a dispute may arise between us and an alliance partner concerning the research, development or commercialization of a program or product candidate resulting in a delay in milestones, royalty payments or termination of a program and possibly resulting in costly litigation or arbitration which may divert management attention and resources; and
- an alliance partner may use our proprietary information or intellectual property in such a way as to invite litigation from a third party or fail to maintain or prosecute intellectual property rights such that our rights in such property are jeopardized.

Specifically, with respect to termination rights, Sanofi may terminate the entire alliance or its current alliance target program for any or no reason upon 30 days' written notice to us. The agreement with Sanofi may also be terminated by either party for material breach by the other party, including a failure to comply with such party's diligence obligations that remains uncured after 120 days. Depending on the timing of any such termination, we may not be entitled to receive the option exercise fees or milestone payments, as these payments terminate with termination of the respective program or agreement. In June 2017, AstraZeneca provided notice to us of its election to terminate our collaboration and license agreement in its entirety, which termination will become effective in June 2018. Upon expiration of the termination period, AstraZeneca's rights to RG-125(AZD4076) will revert to us. We will be responsible for any further development costs at that time.

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

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

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

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

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

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

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

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

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

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

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

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

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

In addition, if our alliance partners elect to pursue the development and commercialization of certain programs, we will lose control over the manufacturing of the product candidate subject to the agreement. For example, if Sanofi elects to develop and commercialize a product candidate targeting miR-21 or miR-221/222 for oncology indications or RG-012 for kidney fibrosis under its strategic alliance with us, Sanofi will be responsible for the manufacture of the product candidates for further clinical trials. Sanofi will be free to use a manufacturer of its own choosing or manufacture the product candidates in its own manufacturing facilities. In such a case, we will have no control over Sanofi's processes or supply chains to ensure the timely manufacture and supply of the product candidates. In addition, we will not be able to ensure that the product candidates will be manufactured under the correct conditions to permit the product candidates to be used in such clinical trials.

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

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

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

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

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

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

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

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

RISKS RELATED TO OUR INTELLECTUAL PROPERTY

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

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

If the patent applications we hold or have in-licensed with respect to our programs or product candidates fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize, future products. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. A patent may be challenged through one or more of several administrative proceedings including post-grant challenges, re-examination or opposition before the U.S. PTO or foreign patent offices. For example, re-examination of, or oppositions to, patents owned by or licensed to us have previously been initiated, and while we believe these concluded proceedings did not result in a commercially relevant impact on the individual patents, any successful challenge of patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we or our strategic alliance partners may develop.

Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, in certain situations, if we and one or more third parties have filed patent applications in the United States and claiming the same subject matter, an administrative proceeding, known as an interference, can be initiated to determine which applicant is entitled to the patent on that subject matter. Such an interference proceeding provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications, or those of our alliance partners or licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of a patent or patent application in such a proceeding may not be successful and, even if successful, may result in substantial costs and distract our management and other employees.

In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords, is limited. Once the patent life has expired for a product, we may be open to competition from generic medications. Further, if we encounter delays in regulatory approvals, the period of time during which we could market a product candidate under patent protection could be reduced.

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

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. If we are unable to prevent material disclosure of the non-patented intellectual

property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

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

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we and our strategic alliance partners are pursuing development candidates. For example, we are aware that Roche Innovation Center Copenhagen has patents and patent applications in the *micro*RNA therapeutics space, including patents and patent applications related to targeting *micro*RNAs, such as miR-122, for the treatment of disease. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

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

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

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

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

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on

reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

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

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

Our defense in a litigation may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

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

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

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

RISKS RELATED TO COMMERCIALIZATION OF PRODUCT CANDIDATES

The commercial success of our programs that are part of our strategic alliance agreements with Sanofi or others will depend in large part on the development and marketing efforts of our alliance partners. If our alliance partners are unable or unwilling to perform in accordance with the terms of our agreements, our potential to generate future revenue from these programs would be significantly reduced and our business would be materially and adversely harmed. *

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

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

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

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

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

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

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

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

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

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

Unless other formulations are developed in the future, we expect our compounds to be formulated in an injectable form. Injectable medications may be disfavored by patients or their physicians in the event drugs which are easy to administer, such as oral medications, are available. If a product is approved, but does not achieve an adequate level of acceptance by physicians, patients and healthcare payors, we may not generate sufficient revenues from such product and we may not become or remain profitable. For example, several new antivirals and antiviral combinations have been approved for the treatment of the Hepatitis C infection since we commenced our HCV program. Such increased competition may decrease any future potential revenue for future product candidates due to increasing pressure for lower pricing and higher discounts in the commercialization of our product.

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

We currently do not have an organization for the sales, marketing and distribution of pharmaceutical products and the cost of establishing and maintaining such an organization may exceed the cost-effectiveness of doing so. In order to market any products that may be approved, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. For example, in order to exercise our co-promotion rights with Sanofi with respect to our miR-21 and miR-221/222 programs, we would need to build our sales, marketing, managerial and other non-technical capabilities in order to effectively carry out sales or co-promotion activities with respect to any approved products that are developed through these programs. With respect to certain of our current programs as well as future programs, we may rely completely on an alliance partner for sales and marketing. In addition, we intend to enter into strategic alliances with third parties to commercialize other product candidates, including in markets outside of the United States or for other large markets that are beyond our resources. Although we intend to establish a sales organization if we are able to obtain approval to market any product candidates for niche markets in the United States, we will also consider the option to enter into strategic alliances for future product candidates in the United States if commercialization requirements exceed our available resources. This will reduce the revenue generated from the sales of these products.

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

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

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

Under our existing strategic alliance agreement, Sanofi will be responsible for the commercialization of current and any future product candidates developed under our programs. If any other product candidates that we develop are approved for commercialization, we may also enter into agreements with third parties to market them on a worldwide basis or in more limited geographical regions. We expect that we will be subject to additional risks related to entering into international business relationships, including:

- different regulatory requirements for drug approvals in foreign countries;
- reduced protection for intellectual property rights;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;

- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geopolitical actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods and fires.

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

Market acceptance and sales of any product candidates that we develop will depend on coverage and reimbursement policies and may be affected by future healthcare reform measures. Government authorities and third party payors, such as private health insurers, government payors and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. We cannot be sure that coverage and adequate reimbursement will be available for any future product candidates. Also, inadequate reimbursement amounts may reduce the demand for, or the price of, our future products. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage for the product. If reimbursement is not available, or is available only at limited levels, we may not be able to successfully commercialize product candidates that we develop.

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

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

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

RISKS RELATED TO OUR BUSINESS OPERATIONS AND INDUSTRY

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

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

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

As of September 30, 2017 we had 61 employees. In connection with our May 2017 corporate restructuring plan, we committed to a reduction in our total workforce by approximately 30% percent to 65 employees. In the future we may expand our employee base to increase our managerial, scientific, operational, commercial, financial and other resources and to hire more consultants and contractors. Future growth would impose significant additional responsibilities on our management, including the need to identify, recruit, maintain, motivate and integrate additional employees, consultants and contractors. Also, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, give rise to operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the development of additional product candidates. Moreover, if our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate and/or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

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

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

We may undertake internal restructuring activities in the future that could result in disruptions to our business or otherwise materially harm our results of operations or financial condition.*

From time to time we may undertake internal restructuring activities as we continue to evaluate and attempt to optimize our cost and operating structure in light of developments in our business strategy and long-term operating plans. For example, we initiated a corporate restructuring in May 2017 that resulted in a reduction in our workforce. Any such restructuring activities may result in write-offs or other restructuring charges. There can be no assurance that any restructuring activities that we have undertaken or undertake in the future will achieve the cost savings, operating efficiencies or other benefits that we may initially expect. Restructuring activities may also result in a loss of continuity, accumulated knowledge and inefficiency during transitional periods and thereafter. In addition, internal restructurings can require a significant amount of time and focus from management and other employees, which may divert attention from commercial operations. If any internal restructuring activities we have undertaken or undertake in the future fail to achieve some or all of the expected benefits therefrom, our business, results of operations and financial condition could be materially and adversely affected.

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

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be directly, or indirectly through our customers, further subject to various federal and state fraud and abuse laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient

privacy regulation by the federal government and by the U.S. states and foreign jurisdictions in which we conduct our business. The healthcare laws and regulations that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, either the referral of an individual, or the purchase or recommendation of an item or service for which payment may be made under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, including the civil False Claims Act, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment to the federal government, including Medicare or Medicaid, that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created additional federal criminal statutes that prohibit, among other things, executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their implementing regulations, which imposes certain requirements on certain types of individuals and entities relating to the privacy, security and transmission of individually identifiable health information;
- the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program, with specific exceptions, to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians, and further requires applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members; and
- state and foreign law equivalents of each of the above federal laws, such as: anti-kickback and false claims laws which may apply to items or services reimbursed by any third party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

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

Recent and future healthcare legislation may further impact our business operations.

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals to change the healthcare system in ways that could affect our ability to sell our products profitably. Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

We expect that healthcare reform measures that may be adopted in the future may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors.

We cannot predict what healthcare reform initiatives may be adopted in the future. Further federal, state and foreign legislative and regulatory developments are likely, and we expect ongoing initiatives to increase pressure on drug pricing. Such reforms could have an adverse effect on anticipated revenues from product candidates that we may successfully develop and for which we may obtain regulatory approval and may affect our overall financial condition and ability to develop product candidates.

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

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

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

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

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

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

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

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

RISKS RELATED TO OUR COMMON STOCK

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

Since January 1, 2014, our closing stock price as reported on The NASDAQ Global Market has ranged from $0.83 to $22.08, through November 3, 2017. The trading price of our common stock is likely to continue to be volatile.

Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in preclinical studies or clinical trials;
- inability to obtain additional funding;
- any delay in filing an IND or NDA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND or NDA;
- failure to maintain our existing strategic alliances or enter into new alliances;
- failure of our strategic alliance partners to elect to develop and commercialize product candidates under our alliance agreements or the termination of any programs under our alliance agreements;
- failure by us or our licensors and strategic alliance partners to prosecute, maintain or enforce our intellectual property rights;
- failure to successfully develop and commercialize our product candidates;
- changes in laws or regulations applicable to our preclinical and clinical development activities, product candidates or future products;
- inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;
- failure to meet or exceed financial projections we may provide to the public;
- failure to meet or exceed the estimates and projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our strategic alliance partners or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- changes in the market valuations of similar companies;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

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

We are an "emerging growth company," and the reduced reporting requirements applicable to emerging growth companies could make our common stock less attractive to investors.

We are currently an "emerging growth company," as defined in the JOBS Act. As an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not "emerging growth companies," including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding

advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We will likely be an "emerging growth company" through December 31, 2017, at which time we will lose that status. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

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

The requirements of being a publicly traded company may strain our resources and divert management's attention.

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

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

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline. In addition, shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans are or may become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and Rule 144 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

Certain holders of our securities are entitled to rights with respect to the registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by our affiliates as defined in Rule 144 under the Securities Act. Pursuant to our registration statements on Form S-3 which became effective in April 2014 and in April 2015, up to 1,272,000 shares held by certain of our stockholders remain available for resale thereunder. We may file additional registration statements in the future to provide for the further sale of shares of common stock by our stockholders. Any further sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

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

We expect that significant additional capital will be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time, any of which may result in material dilution to investors and/or our existing stockholders. New investors could also be issued securities with rights superior to those of our existing stockholders.

Pursuant to our 2012 Equity Incentive Plan, or the 2012 Plan, our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2012 Plan will automatically increase each year by up to 4% of all shares of our capital stock outstanding as of December 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 previously adopted an Inducement Plan pursuant to which our management had the ability to 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 increase the number of shares which may be granted under the Inducement Plan, or adopt another inducement plan for which no stockholder approval is required under applicable rules and regulations, and grant options pursuant to such plan, our stockholders may experience additional dilution, which could cause our stock price to fall.

We may be unable to comply with the applicable continued listing requirements of The NASDAQ Global Market. *

Our common stock is currently listed on The NASDAQ Global Market, or NASDAQ. In order to maintain this listing, we must satisfy minimum financial and other continued listing requirements and standards, including a minimum closing bid price requirement for our common stock of $1.00 per share. There can be no assurance that we will be able to comply with the applicable listing standards. For example, if we were to fail to meet the minimum bid price requirement for 30 consecutive business days, we could become subject to delisting. Although NASDAQ may provide us with a compliance period in which to regain compliance with the minimum bid price requirement, we cannot assure you that we would be able to regain compliance within the period provided by NASDAQ. In order to regain compliance with such requirement, the closing bid price of our common stock would need to meet or exceed $1.00 per share for at least 10 consecutive business days during the compliance period. If we were not able to regain compliance within the allotted compliance period for this requirement or any other applicable listing standard, including any extensions that may be granted by NASDAQ, our shares of common stock would be subject to delisting. In the event that our common stock is delisted from NASDAQ and is not eligible for quotation or listing on another market or exchange, trading of our common stock could be conducted only in the over-the-counter market or on an electronic bulletin board established for unlisted securities such as the Pink Sheets or the OTC Bulletin Board. In such event, it could become more difficult to dispose of, or obtain accurate price quotations for our common stock and there would likely also be a reduction in our coverage by securities analysts and the news media, which could cause the price of our common stock to decline further.

We are the subject of a putative securities class action lawsuit, and additional securities litigation may be brought against us in the future. *

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock price volatility in recent years. On January 31, 2017, a putative class action complaint was filed in the United States District Court for the Southern District of California against us, Paul C. Grint (our former Chief Executive Officer) and Joseph P. Hagan (then our Chief Operating Officer and currently our President and Chief Executive Officer). The complaint includes claims asserted, on behalf of certain purchasers of our securities, under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended. In general, the complaint alleges that between January 21, 2016, and June 27, 2016, the defendants violated the federal securities laws by making materially false and misleading statements regarding our business and the prospects for RG-101, thereby artificially inflating the price of our securities. A second action has subsequently been filed making the same allegations but extending the period of alleged violations to January 27, 2017 and also naming our Chief Research & Development Officer, Timothy M. Wright, as a defendant. The plaintiffs seek unspecified monetary damages and other relief. It is possible that additional lawsuits will be filed, or allegations made by stockholders, with respect to these same or other matters and also naming us and/or our officers and directors as defendants. Due to the early stage of these proceedings, we are not able to predict or reasonably estimate the ultimate outcome or possible losses relating to these claims. While we carry liability insurance, there is no assurance that any losses we incur in connection with the current lawsuits or any future lawsuits will be covered or that coverage, if any, will be sufficient. In addition, the current lawsuits and similar future litigation could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

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

Under Section 382 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change income may be limited. We triggered an "ownership change" limitation at the completion of our initial public offering in October 2012 and again in July 2015. We may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership. As a result, if we earn net taxable income, our ability to use our pre-change net operating loss carryforwards to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

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

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. In addition, our ability to pay cash dividends is currently prohibited by the terms of our secured debt, and any future debt financing arrangement may contain terms prohibiting or limiting the amount of dividends that may be declared or paid on our common stock. Any return to stockholders will therefore be limited to the appreciation of their stock.

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

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

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

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

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

Recent Sales of Unregistered Securities

None.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

None.

ITEM 6. EXHIBITS

Exhibit Number	Description
3.1	Amended and Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Quarterly Report on Form 10-Q, filed with the SEC on August 3, 2016).
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K, filed with the SEC on June 8, 2016).
4.1	Reference is made to Exhibits 3.1 and 3.2.
4.2	Form of Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.1 to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-183384), originally filed with the SEC on August 17, 2012).
31.1	Certification of the Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
31.2	Certification of the Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
32.1*	Certification of the Principal Executive Officer and the Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101.INS	XBRL Instance Document.
101.SCH	XBRL Taxonomy Extension Schema Document.
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document.

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

SIGNATURES

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

Regulus Therapeutics Inc.

Date: November 7, 2017

By: /s/ Joseph P. Hagan

Joseph P. Hagan
President and Chief Executive Officer
(Principal Executive Officer)

Date: November 7, 2017

By: /s/ Daniel R. Chevallard

Daniel R. Chevallard
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Joseph P. Hagan, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Regulus Therapeutics Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13(a)-15(f) and 15(d)-15(f)) for the registrant and have:

a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c. evaluated the effectiveness of the registrant’s disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. disclosed in this report any change in the registrant’s internal control over financial reporting that occurred during the registrant’s most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant’s internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant’s auditors and the audit committee of the registrant’s board of directors (or persons performing the equivalent functions):

a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant’s ability to record, process, summarize and report financial information; and

b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant’s internal control over financial reporting.

Date: November 7, 2017

/s/ Joseph P. Hagan
Joseph P. Hagan
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF PRINCIPAL FINANCIAL OFFICER
PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Daniel R. Chevallard, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Regulus Therapeutics Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13(a)-15(f) and 15(d)-15(f)) for the registrant and have:

a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: November 7, 2017

/s/ Daniel R. Chevallard

Daniel R. Chevallard
Chief Financial Officer
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the quarterly report of Regulus Therapeutics Inc. (the "Company") on Form 10-Q for the quarter ended September 30, 2017 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Joseph P. Hagan, President and Chief Executive Officer, and I, Daniel R. Chevallard, Principal Financial and Accounting Officer, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: November 7, 2017

/s/ Joseph P. Hagan
Joseph P. Hagan
President and Chief Executive Officer
(Principal Executive Officer)

Date: November 7, 2017

/s/ Daniel R. Chevallard
Daniel R. Chevallard
Chief Financial Officer
(Principal Financial and Accounting Officer)

The foregoing certification is being furnished solely pursuant to 18 U.S.C. Section 1350 and is not being filed as part of the Report or as a separate disclosure document and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Report), irrespective of any general incorporation language contained in such filing.