Regulus Therapeutics Inc.
Form 10-Q
November 09, 2018

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549
FORM 10-Q
(Mark One)
x QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE QUARTERLY PERIOD ENDED SEPTEMBER 30, 2018
or
¨ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE TRANSITION PERIOD FROM TO
Commission file number: 001-35670
Regulus Therapeutics Inc.
(Exact name of registrant as specified in its charter)

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

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

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No ¨
Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes x No ¨
Indicate by check mark whether registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, 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	x
Non-accelerated filer	¨	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 ý
As of November 2, 2018, the registrant had 8,750,343 shares of Common Stock ($0.001 par value) outstanding.

REGULUS THERAPEUTICS INC.
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PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

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

	September 30, 2018 (Unaudited)	December 31, 2017
Assets		
Current assets:		
Cash and cash equivalents	$ 14,084	$ 13,519
Short-term investments	6,433	46,555
Contract and other receivables	13	373
Prepaid materials, net	4,194	4,783
Prepaid expenses and other current assets	717	1,506
Total current assets	25,441	66,736
Property and equipment, net	8,324	9,708
Intangibles, net	676	775
Other assets	327	590
Total assets	$ 34,768	$ 77,809
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	$ 1,235	$ 5,743
Accrued liabilities	1,856	2,995
Accrued compensation	1,292	1,985
Current portion of term loan, less debt issuance costs	19,069	19,859
Current portion of contract liabilities	72	—
Other current liabilities	2,130	2,018
Total current liabilities	25,654	32,600
Contract liabilities, less current portion	24	1,921
Deferred rent, less current portion	7,139	8,072
Other long-term liabilities	373	—
Total liabilities	33,190	42,593
Commitments and Contingencies		
Stockholders' equity:		
Common stock, $0.001 par value; 200,000,000 shares authorized, 8,750,343 and 8,662,435 shares issued and outstanding at September 30, 2018 (unaudited) and December 31, 2017, respectively	9	9
Additional paid-in capital	385,793	381,199
Accumulated other comprehensive loss	(63)	(134)
Accumulated deficit	(384,161)	(345,858)
Total stockholders' equity	1,578	35,216
Total liabilities and stockholders' equity	$ 34,768	$ 77,809

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,	
	2018	2017	2018	2017
	(Unaudited)			
Revenues:				
Revenue under strategic alliances and collaborations	$18	$18	$54	$54
Total revenues	18	18	54	54
Operating expenses:				
Research and development	6,879	12,697	28,720	42,727
General and administrative	2,993	2,736	10,115	13,752
Total operating expenses	9,872	15,433	38,835	56,479
Loss from operations	(9,854)	(15,415)	(38,781)	(56,425)
Other income (expense):				
Interest and other income	201	160	483	559
Interest and other expense	(620)	(580)	(1,848)	(1,730)
Loss before income taxes	(10,273)	(15,835)	(40,146)	(57,596)
Income tax benefit	—	7	—	139
Net loss	$(10,273)	$(15,828)	$(40,146)	$(57,457)
Other comprehensive loss:				
Unrealized gain (loss) on short-term investments, net	16	(16)	70	19
Comprehensive loss	$(10,257)	$(15,844)	$(40,076)	$(57,438)
Net loss per share, basic and diluted	$(1.18)	$(2.11)	$(4.62)	$(10.52)
Weighted average shares used to compute basic and diluted net loss per share	8,703,626	7,506,529	8,688,831	5,463,096

See accompanying notes to these condensed financial statements.

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

	Nine months ended September 30,	
	2018	2017
	(Unaudited)	
Operating activities		
Net loss	$(40,146)	$(57,457)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization expense	1,672	1,942
Stock-based compensation	4,374	6,531
Amortization of premium on investments, net	92	271
Other	182	206
Change in operating assets and liabilities:		
Contracts and other receivables	360	1,124
Prepaid materials	589	(360)
Prepaid expenses and other assets	1,050	2,405
Accounts payable	(4,509)	(579)
Accrued liabilities	(1,138)	(652)
Accrued compensation	(693)	(631)
Contract liabilities	(54)	(54)
Deferred rent and other liabilities	(1,035)	(418)
Net cash used in operating activities	(39,256)	(47,672)
Investing activities		
Purchases of short-term investments	—	(48,539)
Sales and maturities of short-term investments	40,101	58,310
Purchases of property and equipment	(22)	(217)
Acquisition of intangibles	—	(16)
Net cash provided by investing activities	40,079	9,538
Financing activities		
Proceeds from issuance of common stock, net	219	43,411
Proceeds from exercise of common stock options	2	4
Principal payments on other long-term obligations	(833)	—
Proceeds from capital lease financing	354	—
Net cash used in financing activities	(258)	43,415
Net increase in cash and cash equivalents	565	5,281
Cash and cash equivalents at beginning of period	13,519	14,941
Cash and cash equivalents at end of period	$14,084	$20,222
Supplemental disclosure of cash flow information		
Interest paid	$(1,573)	$(1,444)
Income taxes paid	$(1)	$(1)
Supplemental disclosure of non-cash investing and financing activities		
Non-cash acquisition of property and equipment	$306	$—

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, 2017, from which the balance sheet information herein was derived.

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 reduced our total workforce by approximately 30%, to approximately 65 employees. We completed the workforce reduction in June 2017. In July 2018, we implemented a second corporate restructuring to further reduce operating expenses and focus our resources, which involved an additional reduction in our workforce of approximately 60%. The workforce reduction was substantially completed in July 2018. As of September 30, 2018, we had 25 employees.

On October 2, 2018 we filed a Certificate of Amendment of Amended and Restated Certificate of Incorporation with the Secretary of State of the state of Delaware to effect a 1-for-12 reverse stock split of our issued and outstanding common stock. The reverse stock split became effective at 5:00 p.m. Eastern Time on October 3, 2018 and our common stock began trading on a split-adjusted basis on The Nasdaq Global Market on October 4, 2018. The accompanying condensed financial statements and notes thereto give retrospective effect to the reverse stock split for all periods presented. All issued and outstanding common stock, options exercisable for common stock, restricted stock units, and per share amounts contained in our condensed financial statements have been retrospectively adjusted.

Liquidity

The accompanying financial statements have been prepared on a basis which assumes we are a going concern, and does not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classifications of liabilities that may result from any uncertainty related to our ability to continue as a going concern. Through the date of the issuance of these financial statements, we have principally been financed through proceeds received from the sale of our common stock and other equity securities, debt financings, up-front payments and milestones received from collaboration agreements. As of September 30, 2018, we had approximately $20.5 million of cash, cash equivalents and short-term investments. Based on our operating plans, we believe our cash, cash equivalents and short-term investments may not be sufficient to fund our operations for the period one year following the issuance of these financial statements. As a result, there is substantial doubt about our ability to continue as a going concern. All amounts due under the Term Loan (see note 5) have been classified as a current liability as of September 30, 2018 and December 31, 2017 due to the considerations discussed above and the assessment that the material adverse change clause under the Term Loan is not within our control. We have not been notified of an event of default by the Lender as of the date of the filing of this Form 10-Q.

We intend to seek additional capital through equity and/or debt financings, collaborative or other funding arrangements with partners or through other sources of financing. Should we seek additional financing from outside

sources, we may not be able to raise such financing on terms acceptable to us, or at all. If we are unable to raise additional capital when required or on acceptable terms, we may be required to scale back or discontinue the advancement of product candidates, reduce headcount, file for bankruptcy, reorganize, merge with another entity, or cease operations.

If we become unable to continue as a going concern, we may have to liquidate our assets, and might realize significantly less than the values at which they are carried on our financial statements, and stockholders may lose all or part of their investment in our common stock.

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.

Effective January 1, 2018, we adopted Accounting Standards Update ("ASU") 2014-09, Revenue from Contracts with Customers (Topic 606) ("Topic 606") using the modified retrospective method which consisted of applying and recognizing the cumulative effect of Topic 606 at the date of initial application. Topic 606 supersedes the revenue recognition requirements in Accounting Standards Codification ("ASC") Topic 605, Revenue Recognition ("Topic 605"). All periods prior to the adoption date of Topic 606 have not been restated to reflect the impact of the adoption of Topic 606, but are accounted for and presented under Topic 605.

The following paragraphs in this section describe our revenue recognition accounting polices under Topic 606 upon adoption on January 1, 2018. Refer to Note 1 to the financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017 for revenue recognition accounting policies under Topic 605.

We recognize revenue when we transfer promised goods or services to customers in an amount that reflects the consideration to which we expect to be entitled in exchange for those goods or services. To determine revenue recognition for contracts with customers we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligation(s) in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligation(s) in the contract; and (v) recognize revenue when (or as) we satisfy the performance obligation(s). At contract inception, we assess the goods or services promised within each contract, assess whether each promised good or service is distinct and identify those that are performance obligations. We recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

Collaborative Arrangements

We enter into collaborative arrangements with partners that typically include payment to us of one of more of the following: (i) license fees; (ii) payments related to the achievement of developmental, regulatory, or commercial milestones; and (iii) royalties on net sales of licensed products. Where a portion of non-refundable up-front fees or other payments received are allocated to continuing performance obligations under the terms of a collaborative arrangement, they are recorded as contract liabilities and recognized as revenue when (or as) the underlying performance obligation is satisfied.

As part of the accounting for these arrangements, we must develop estimates and assumptions that require judgment to determine the underlying stand-alone selling price for each performance obligation which determines how the transaction price is allocated among the performance obligation(s). The stand-alone selling price may include items such as forecasted revenues, development timelines, discount rates, and probabilities of technical and regulatory success. We evaluate each performance obligation to determine if it can be satisfied at a point in time, or over time. In addition, variable consideration must be evaluated to determine if it is constrained and, therefore, excluded from the transaction price.

License Fees

If a license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenues from non-refundable, up-front fees allocated to the license when the license is transferred to the licensee and the licensee is able to use and benefit from the license. For licenses that are bundled with other performance obligations, we use judgment to assess the nature of the combined performance obligation to determine whether it is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue. We evaluate the measure of progress each reporting period and, if

necessary, adjust the measure of performance and related revenue recognition.

Milestone Payments

At the inception of each arrangement that includes milestone payments (variable consideration), we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price. If it is probable that a milestone event would occur at the inception of an arrangement, the associated milestone value is included in the transaction price. Milestone payments that are contingent upon the achievement of events that are uncertain or not controllable, such as regulatory approvals, are generally not considered probable of being achieved until those approvals are received, and therefore not included in the transaction price. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each reporting period, we evaluate the probability of achievement of such milestones and any related constraint(s), and if necessary, may adjust our estimate of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect license, collaboration or other revenues and earnings in the period of adjustment.

Royalties

For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and for which the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any royalty revenue resulting from any of our collaborative arrangements.

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 restricted stock units by determining the fair value of each restricted stock unit based on the closing market price of our common stock on the date of grant. We recognize stock-based compensation expense using the accelerated multiple-option approach over the requisite service periods of the awards.

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.

Recent Accounting Pronouncements

As disclosed above, effective January 1, 2018, we adopted Topic 606. Since ASU 2014-09 was issued, several additional ASUs have been issued and incorporated within Topic 606 to clarify various elements of the guidance. As part of our adoption efforts, we have completed the assessment of our collaboration and license agreements under Topic 606. We adopted Topic 606 in the first quarter of 2018 using the modified retrospective method which consists of applying and recognizing the cumulative effect of Topic 606 at the date of initial application and providing certain additional disclosures as defined per Topic 606. On January 1, 2018, we recorded a cumulative adjustment to decrease deferred revenue and accumulated deficit by approximately $1.8 million to reflect the impact of the adoption of Topic 606. The cumulative adjustment relates primarily to our agreement with Sanofi which is described further in Note 7.

Below is a summary of the affected line items of the condensed balance sheets upon adoption of Topic 606 (in thousands):

	Balance at December 31, 2017	Adjustments due to Topic 606	Balance at January 1, 2018
Balance Sheet			
Deferred revenue (contract liabilities), non-current	1,921	(1,844)	77
Accumulated deficit	(345,858)	1,844	(344,014)

There is no difference between what our revenue would have been in the three and nine months ended September 30, 2018, reported under Topic 606 or Topic 605.

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. The adoption of this guidance had 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. Since ASU 2016-02 was issued, several additional ASUs have been issued to clarify various elements of the guidance. 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 in the process of determining the impact the adoption will have on our financial statements and expect significant changes to the recognition of right-of-use assets and liabilities associated with our operating leases.

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 had 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. The adoption of this guidance will have no 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 had no impact on our financial statements and will continue to have no impact on our financial statements unless we have modification accounting in accordance with Topic 718.

In December 2017, The Tax Cuts and Jobs Act (the "Act") was signed into law and amended the Internal Revenue Code, or IRC, to reduce tax rates and modify policies, credits, and deductions for individuals and businesses. Due to uncertainties which currently exist in the interpretation of the provisions of the Act regarding IRC Section 162(m), as of September 30, 2018, we have not completed our evaluation of the potential impacts of IRC Section 162(m) as amended by the Act on our financial statements. In March 2018, the FASB issued ASU No. 2018-05, Income taxes (Topic 740): Amendments to SEC Paragraphs Pursuant to SEC Staff Accounting Bulletin No. 118, which provides guidance regarding the recording of tax impacts where uncertainty exists, in the period of adoption of the Act. To the extent that a company's accounting for certain income tax effects of the Act is incomplete but it is able to determine a reasonable estimate, it must record a provisional estimate to be included in the condensed financial statements. If a company cannot determine a provisional estimate to be included in the condensed financial statements, it should continue to apply ASC 740 on the basis of the provision of the tax laws that were in effect immediately before the enactment of the Act. We have provisionally determined that there is no deferred tax benefit or expense with respect to the re-measurement of certain deferred tax assets and liabilities due to the full valuation allowance against net deferred tax assets. Additional analysis of the law and the impact to the company will be performed and any impact will be recorded in the respective quarter.

In June 2018, the FASB issued ASU No. 2018-07, Compensation - Stock Compensation: Improvements to Nonemployee Share-Based Payment Accounting, which aligns the measurement and classification guidance for share-based payment to non-employees with the guidance for share-based payments to employees. Under the new guidance, the measurement period for equity-classified non-employee awards will be fixed at the grant date. This update is effective for annual periods beginning after December 15, 2018, and interim periods within those periods and early adoption is permitted. The adoption of this guidance will have no impact on our financial statements.

In August 2018, the FASB issues ASU No. 2018-13, Fair Value Measurement (Topic 820): Disclosure Framework - Changes to the Disclosure Requirements for Fair Value Measurement, which updates and modifies the disclosure requirements on fair value measurements in Topic 820, primarily in relation to Level 3 fair value measurements. This update is effective for annual periods beginning after December 15, 2019, and interim periods within those periods. Early adoption is permitted. The adoption of this guidance will have no impact on our financial statements.

2. Net Loss Per Share

Basic net loss per share is calculated by dividing net loss by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents. Diluted net loss per share is calculated by dividing net loss 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 zero and 575,256 shares attributable to common stock options and restricted stock units ("RSUs") for the three and nine months ended September 30, 2018, respectively, compared to 106,597 and 210,816 shares attributable to common stock options for the three and nine months ended September 30, 2017, respectively.

3. Investments

We invest our excess cash primarily in debt instruments of financial institutions, corporations, U.S. government-sponsored agencies and the U.S. Treasury. We generally hold our investments to maturity and do not sell our investments before we have recovered our amortized cost basis.

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

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	Maturity (in years)	Amortized cost	Unrealized Gains	Unrealized Losses	Estimated fair value
As of September 30, 2018					
Certificates of deposit	1 or less	$ 2,440	$ —	$ —	$ 2,440
U.S. Treasury securities	1 or less	3,999	1	(7)	3,993
Total		$ 6,439	$ 1	$ (7)	$ 6,433

	Maturity (in years)	Amortized cost	Unrealized Gains	Unrealized Losses	Estimated fair value
As of December 31, 2017					
Corporate debt securities	1 or less	$ 32,922	$ —	$ (55)	$ 32,867
Certificates of deposit	1 or less	8,216	—	—	8,216
U.S. Treasury securities	1 or less	3,996	—	(18)	3,978
Debt securities of U.S. government-sponsored agencies	1 or less	1,498	—	(4)	1,494
Total		$ 46,632	$ —	$ (77)	$ 46,555

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, 2018 and December 31, 2017 (in thousands):

	Fair value as of September 30, 2018			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$13,631	$13,631	$—	$ —
Certificates of deposit	2,440	—	2,440	—
U.S. treasury securities	3,993	—	3,993	—
	$20,064	$13,631	$6,433	$ —

	Fair value as of December 31, 2017			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents	$10,847	$10,847	$—	$ —
Corporate debt securities	32,867	—	32,867	—
Certificates of deposit	8,216	—	8,216	—
U.S. treasury securities	3,978	—	3,978	—
Debt securities of U.S. government-sponsored agencies	1,494	—	1,494	—
	$57,402	$10,847	$46,555	$ —

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" or sometimes referred to as the "Lender"), 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, and no amounts were borrowed under the Term B Loan. 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 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%. Under the original Loan Agreement, we were required to make interest-only payments through June 1, 2018, followed by 24 equal monthly payments of principal and unpaid accrued interest.

In March 2018, we and Oxford entered into an amendment to our Loan Agreement, providing for the modification of the loan amortization period from a 24-month period commencing on July 1, 2018 to a 15-month period commencing on April 1, 2019, subject to our receipt, following the date of the amendment, of unrestricted net cash proceeds of not less than $30.0 million on or prior to June 30, 2018. The ability to modify the loan amortization period under this amendment to the Loan Agreement expired on June 30, 2018, as we did not receive unrestricted net cash proceeds of not less than $30.0 million on or prior to June 30, 2018.

In August 2018, we and Oxford entered into an additional amendment to our Loan Agreement, providing for a modification of the loan amortization period. Under the terms of the amendment, principal amortization and repayment was deferred between August 2018 through October 2018, and during this period, we were required to make payments of interest-only. Amortization payments will recommence in November 2018. In addition, the amendment contained a minimum cash reserve covenant, whereby we will be required to maintain aggregate cash reserves of not less than 110% of the principal balance of the Term Loan that would be outstanding on such date that our then-held cash reserves would first be completely exhausted based on certain assumptions specified in the

amendment. There were no changes to the maturity date of the Term Loan, which is June 2020. Pursuant to the amendment, we granted the Lender a security interest in our intellectual property as additional collateral for the repayment of the Term Loan.

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 and certain assets under capital lease obligations. We have also agreed not to encumber our intellectual property assets, except as permitted by the Loan Agreement. The Loan Agreement includes customary events of default, including instances of a material adverse change in our operations, that may require prepayment of the outstanding Term Loan. All amounts due under the Term Loan have been classified as a current liability as of September 30, 2018 due to the considerations discussed in Note 1 and the assessment that the material adverse change clause under the Term Loan is not within our control. We have not been notified of an event of default by the Lender as of the date of the filing of this Form 10-Q.

As of September 30, 2018, we had a net liability of $19.1 million outstanding under the Term Loan. 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, 2018, we were in compliance with all covenants under the Loan Agreement.

As of September 30, 2018, future principal payments for the Term Loan due under the Loan Agreement are as follows (in thousands):

2018	$1,917
2019	11,500
2020	5,750
	$19,167

6. Stockholders' Equity

Shares Reserved for Future Issuance

The following shares of common stock were reserved for future issuance as of September 30, 2018 (in thousands):

Common stock options outstanding	1,134
RSUs outstanding	66
Common stock available for future grant under 2012 Equity Incentive Plan	61
Common stock available for future grant under 2015 Inducement Plan	3
Employee Stock Purchase Plan	155
Total common shares reserved for future issuance	1,419

The following table summarizes our stock option and RSU activity (together Stock Awards) under all equity incentive plans for the nine months ended September 30, 2018 (shares in thousands):

	Number of options	Weighted average exercise price	Number of RSUs	Weighted average grant date fair value
Stock Awards outstanding at December 31, 2017	887	$ 53.24	35	$ 10.68
Granted	603	$ 11.70	102	$ 3.88
Exercised (options) or Vested (RSUs)	(1)	$ 4.56	(57)	$ 6.25
Canceled/forfeited/expired	(355)	$ 58.59	(8)	$ 7.57
Stock Awards outstanding at September 30, 2018	1,134		72	

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Stock-Based Compensation

The following table summarizes the weighted average assumptions used to estimate the fair value of stock options and performance stock awards granted 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,	
	2018	2017	2018	2017
Stock options				
Risk-free interest rate	2.9%	1.9%	2.7%	2.0%
Volatility	92.0%	89.5%	87.8%	89.4%
Dividend yield	—	—	—	—
Expected term (years)	6.1	6.1	6.1	6.1
Performance stock options				
Risk-free interest rate	—	—	2.7%	2.1%
Volatility	—	—	87.4%	89.9%
Dividend yield	—	—	—	—
Expected term (years)	0.0	0.0	5.7	5.6
Employee stock purchase plan shares				
Risk-free interest rate	2.0%	1.0%	1.8%	0.8%
Volatility	99.9%	104.5%	91.7%	110.7%
Dividend yield	—	—	—	—
Expected term (years)	0.5	0.5	0.5	0.5

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

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
Research and development	$491	$653	$1,745	$2,411
Research and development-restructuring related adjustments	31	—	31	(1,399)
General and administrative	883	631	2,613	2,840
General and administrative-restructuring related adjustments	(15)	—	(15)	2,679
Total	$1,390	$1,284	$4,374	$6,531

7. Strategic Alliances and Collaborations

Revenue recognized from our strategic alliances and collaborations was less than $0.1 million for each of the three and nine months ended September 30, 2018 and 2017.

Sanofi

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

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In June 2013, the original research term expired, upon which we and Sanofi entered into an option agreement pursuant to which Sanofi was granted an exclusive right to negotiate the co-development and commercialization of certain of our unencumbered microRNA programs and we were granted the exclusive right to negotiate with Sanofi for co-development and commercialization of certain miR-21 anti-miRs in oncology and Alport syndrome. In July 2013, we received an upfront payment of $2.5 million, of which $1.25 million is creditable against future amounts payable by Sanofi to us under any future co-development and commercialization agreement we enter pursuant to the option agreement. Revenue associated with the creditable portion of this option payment was deferred as of December 31, 2017 and recorded as an adjustment to accumulated deficit upon our adoption of ASC 606 on January 1, 2018. The non-creditable portion of this payment, $1.25 million, was recognized as revenue over the option period from the effective date of the option agreement in June 2013 through the expiration of the option period in January 2014.

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

In connection with the 2014 Sanofi Amendment, we entered into a Common Stock Purchase Agreement (the "Purchase Agreement"), pursuant to which we sold 1,303,780 shares of our common stock to Aventisub LLC ("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. 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, 2018, contract liabilities associated with the Purchase Agreement and the 2014 Sanofi Amendment was $0.1 million, which we are expecting to recognize over the remaining estimated period of performance of approximately one year.

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.

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 each of the three and nine months ended September 30, 2018 and 2017.

9. Subsequent Events

Reverse Stock Split

On October 2, 2018, we filed a Certificate of Amendment of Amended and Restated Certificate of Incorporation with the Secretary of State of the state of Delaware to effect a 1-for-12 reverse stock split of our issued and outstanding common stock. The primary purpose of the reverse stock split was to raise the per share trading price of our common stock to seek to maintain the listing of our common stock on The Nasdaq Global Market. At the effective time of the reverse stock split at 5:00 p.m. on October 3, 2018, each 12 shares of our issued and outstanding common stock were automatically combined and converted into one issued and outstanding share of common stock. All of our stock options and RSUs outstanding immediately prior to the reverse stock split were proportionately adjusted. All issued and outstanding common stock, options exercisable for common stock, restricted stock units, and per share amounts contained in our condensed financial statements have been retrospectively adjusted.

Tender Offer

On October 15, 2018, we filed a tender offer statement on Schedule TO with the Securities and Exchange Commission related to an offer by us to certain eligible optionholders, subject to specified conditions, to exchange some or all of their outstanding options to purchase shares of our common stock for new RSUs (the "Exchange Offer"). The Exchange Offer will expire at 5:00 p.m., U.S. Pacific Time, on November 11, 2018, unless extended.

An option holder will be eligible to exchange their options (an “Eligible Holder”) if:

- on the date the Exchange Offer commences, either an optionholder is employed by us (each, an “Employee”) or is a non-employee member (each, a “Non-Employee Director”) of our board of directors and has not been notified by us that such optionholder’s employment or service relationship with us is being terminated; and
- such optionholder continues to be an Employee or serve as a Non-Employee Director and has not submitted a notice of resignation or received a notice of termination, as of the first business day following the Expiration Time (as defined in the Exchange Offer).

An option will be eligible for exchange (an “Eligible Option”) if it:

- is held by an Eligible Holder;
- has an exercise price equal to or greater than $4.56 (and an exercise price greater than the closing price of our common stock on the last business day before the Expiration Time); and
- was granted under our 2009 Equity Incentive Plan, 2012 Equity Incentive Plan or 2015 Inducement Plan.

The exchange ratio for each Eligible Option will be determined using the Black-Scholes option pricing model and will be based on, among other things, the fair market value of a share of our common stock, the volatility of our common stock, U.S. treasury rates, the exercise prices of the Eligible Options, the remaining terms of the Eligible Options and the term of the new RSUs. For purposes of determining the fair value of Eligible Options, the fair market value of a share of our common stock will be determined based on the trailing 20-day volume weighted average price (the “20-Day VWAP”). The 20-Day VWAP represents the simple arithmetic average of the daily VWAPs over the 20 consecutive trading days beginning on October 15, 2018 and ending on the last business day prior to the Expiration Time. For purposes of determining the fair value of the new RSUs, the fair market value of a share of our common stock will be determined based on the closing trading price of a share of our common stock on Nasdaq on the last business day prior to the Expiration Time. In no event will an Eligible Optionholder be eligible to receive more new RSUs than the number of shares underlying the number of Eligible Options.

The foregoing is only a summary of the Exchange Offer, does not purport to be complete and is qualified in its entirety by reference to the full text of the Schedule TO, which was filed with the Securities and Exchange Commission on October 15, 2018.

First Amendment to Second Amended and Restated Collaboration and License Agreement

On November 5, 2018, we entered into an amendment to the 2014 Sanofi Amendment with Sanofi to modify the parties' rights and obligations with respect to our miR-21 programs, including our RG-012 program (the "2018 Sanofi Amendment").

Under the terms of the 2018 Sanofi Amendment, we have granted Sanofi a worldwide, royalty-free, fee-bearing, exclusive license, with the right to grant sublicenses, under our know-how and patents to develop and commercialize miR-21 compounds and products for all indications, including Alport Syndrome. Sanofi will control and will assume all responsibilities and obligations for developing and commercializing each of our miR-21 programs, including our obligations regarding the

administration and expense of clinical trials and all other costs, including in-license royalties and other in-license payments, related to our miR-21 programs. Under the terms of the 2018 Sanofi Amendment, we have assigned to Sanofi certain agreements and all materials directed to miR-21 or to any miR-21 compound or product and are required to provide reasonable technical assistance to Sanofi for a period of 24 months after the date of the 2018 Sanofi Amendment.

Under the terms of the 2018 Sanofi Amendment, we are eligible to receive approximately $6.8 million in upfront payments and a payment for miR-21 program-related materials (collectively, the “Upfront Amendment Payments”). We are also eligible to receive up to $40.0 million in development milestone payments. In addition, Sanofi has agreed to reimburse us for certain out-of-pocket transition activities and assume our upstream license royalty obligations. We and Sanofi also agreed to a general release of claims against each other for any claims that arose at any time prior to the date of the 2018 Sanofi Amendment, or that thereafter could arise based on anything that occurred prior to the date of the 2018 Sanofi Amendment.

Fourth Amendment to Loan and Security Agreement

On November 5, 2018 and in connection with the 2018 Sanofi Amendment we entered into a fourth amendment to the Term Loan with the Lender (the "Fourth Amendment").

Under the terms of the Fourth Amendment, the Lender has consented to the 2018 Sanofi Amendment and our license, assignment and transfer to Sanofi of certain of our intellectual property, as required to be delivered to Sanofi under the 2018 Sanofi Amendment (the “Assigned Assets”), which previously served as collateral under the loan and security agreement, and has released its liens in the Assigned Assets, provided that the Lender will continue to have liens on all proceeds received by us pursuant to the Sanofi License. Under the terms of the Fourth Amendment, we now have the option to prepay part of the Term Loan at any time and in any amount after 10 days’ prior written notice. We are also required to prepay part of the Term Loan with 25% of certain payments we receive under the 2018 Sanofi Amendment, which payments consist of the Upfront Amendment Payments and the first development milestone payment in the amount of $10.0 million. We will be required to pay the applicable 5.5% final payment fee related to each such 2018 Sanofi Amendment prepayment. Under the Fourth Amendment, we are required to maintain cash in a collateral account controlled by the Lender of (i) $10.0 million, if we have not received net proceeds of at least $15.0 million from (a) the issuance and sale of our unsecured subordinated convertible debt and/or equity securities or (b) upfront or milestone payments in connection with a joint venture, collaboration or other partnering transaction, other than pursuant to the Sanofi License (the receipt of such net proceeds, a “Capital Event”), or (ii) $5.0 million if a Capital Event has occurred.

The maturity date of the Term Loan remains unchanged and the Term Loan is required to be paid in full on June 1, 2020.

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, 2017 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, 2017, or Annual Report, filed with the Securities and Exchange Commission on March 8, 2018. 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 contains “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. For these forward-looking statements, we claim the protection 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 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;
- the potential election of any strategic alliance or collaboration partner to pursue development and commercialization of any programs or product candidates that are subject to a collaboration with such partner;
- 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 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.

In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

OVERVIEW

We are a clinical-stage biopharmaceutical company focused on discovering and developing first-in-class drugs targeting microRNAs 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 microRNAs pursuant to a license and collaboration agreement. Our most advanced product candidates are RG-012 and RGLS4326. RG-012 is an anti-miR targeting miR-21 for the treatment of Alport syndrome, a life-threatening kidney disease with no approved therapy available. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi, which will be responsible for all costs incurred in the development of our miR programs. RGLS4326 is an anti-miR targeting miR-17 for the treatment of autosomal dominant polycystic kidney disease, or ADPKD. In addition to these clinical programs, we

continue to develop a pipeline of preclinical drug product candidates.

microRNAs 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 microRNAs is directly linked to many diseases. Furthermore, many different infectious pathogens interact and bind to host microRNA to survive. To date, over 500 microRNAs 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 microRNA provides a new therapeutic approach for treating complex diseases.

RNA plays an essential role in the process used by cells to encode and translate genetic information from deoxyribonucleic acid, or DNA, to proteins. RNA is comprised of subunits called nucleotides and is synthesized from a DNA template by a process known as transcription. Transcription generates different types of RNA, including messenger RNAs that carry the information for proteins in the sequence of their nucleotides. In contrast, microRNAs are RNAs that do not code for proteins but rather are responsible for regulating gene expression by modulating the translation and decay of target messenger RNAs. By interacting with many messenger RNAs, a single microRNA 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 microRNAs to regulate the cellular environment for survival. In some instances, the host microRNAs are essential for the replication and/or survival of the pathogen. For example, miR-122 is a microRNA expressed in human hepatocytes and is a key factor for the replication of the hepatitis C virus, or HCV.

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

- microRNAs play a critical role in regulating biological pathways by controlling the translation of many target genes;
- microRNA 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 microRNAs (host and pathogen encoded) to enable their replication and suppression of host immune responses; and
- microRNA therapeutics may be synergistic with other therapies because of their different mechanism of action.

We have assembled significant expertise in the microRNA field, including expertise in microRNA biology and oligonucleotide chemistry, a broad intellectual property estate, relationships with key opinion leaders and a disciplined drug discovery and development process. We are using our microRNA expertise to develop chemically modified, single-stranded oligonucleotides that we call anti-miRs to modulate microRNAs and address underlying disease. We believe microRNAs 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 microRNA biomarkers may be used to select optimal patient segments in clinical trials and to monitor disease progression or relapse. We believe these microRNA biomarkers can be applied toward drugs that we develop and drugs developed by other companies with which we partner or collaborate.

Development Stage Pipeline

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

RG-012: In the third quarter of 2017, we initiated HERA, the Phase II randomized (1:1), double-blinded, placebo-controlled clinical trial 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 pharmacokinetics, or PK, target engagement and downstream effects on genomic disease biomarkers. In December 2017, we concluded our global ATHENA natural history of disease study. In May 2017, we completed a Phase I multiple-ascending dose, or MAD, clinical trial in 24 healthy volunteers (six-week repeat dosing) to determine safety, tolerability and PK of RG-012 prior to chronic dosing in patients. In Phase I clinical trials to date, RG-012 was well-tolerated, and there were no serious adverse events, or SAEs, reported. Preliminary results from the first patients

through the renal biopsy study are encouraging, with kidney tissue concentrations achieved that would be predictive of therapeutic benefit based on animal disease models. In addition, modulation of the target, miR-21, was observed. RG-012 has received orphan designation in both the United States and Europe. In July 2018, in connection with our corporate restructuring, we paused recruitment activities for our RG-012 clinical program in Alport syndrome while we engaged in discussions with Sanofi regarding the potential restructuring of our collaboration. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program to Sanofi, which will be responsible for all costs incurred in the development of our miR-21 programs.

RGLS4326: RGLS4326 is a novel oligonucleotide designed to inhibit miR-17 using a unique chemistry designed to preferentially deliver to the kidney. Preclinical studies with RGLS4326 have demonstrated a reduction in kidney cyst formation, improved kidney weight/body weight ratio, decreased cyst cell proliferation and preserved kidney function in mouse models of ADPKD. In March 2018, we completed dose escalation of a Phase I single ascending dose, or SAD, clinical trial in healthy volunteers and found RGLS4326 was well tolerated and no SAEs were reported. In April 2018, we initiated a Phase I randomized, double-blind, placebo-controlled, MAD clinical trial in healthy volunteers designed to characterize the safety, tolerability, pharmacokinetics and pharmacodynamics of multiple doses of RGLS4326. In July 2018, we voluntarily paused this study due to unexpected observations in our 27-week mouse chronic toxicity study, which was designed to support the Phase II proof-of-concept clinical trial in ADPKD previously planned to start in mid-2019. The observations in the mouse chronic toxicity study were unexpected, given the favorable safety profile of RGLS4326 in previous 7-week non-GLP and GLP toxicity studies in mouse and non-human primates required for Phase I testing, which had no significant findings across similar dose levels and frequencies. In September 2018, we initiated a new mouse chronic toxicity study with several changes believed to address the unexpected findings in the earlier terminated chronic mouse toxicity study. Data from the new study are anticipated in the first quarter of 2019.
RG-125(AZD4076): In June 2017, AstraZeneca AB, or 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 May 2018, AstraZeneca requested to extend the Collaboration and License Agreement termination effective date by an additional 12 months to allow AstraZeneca to complete all activities involving AZD4076. By the end of this 12-month extension, the parties will complete the transfer activities contemplated by the agreement. The new termination effective date pursuant to the extension will be June 2019.
Preclinical Pipeline

A major focus of our preclinical research has historically targeted dysregulated microRNAs 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. We also have early discovery programs investigating additional microRNA targets for infectious diseases, immunology and indications for which there is microRNA dysregulation or in disease settings where the host microRNAs are essential for the replication and/or survival of the pathogen.

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

Hepatitis B virus program: We have determined that advancing our preclinical programs targeting the Hepatitis B virus ("HBV") represents an attractive opportunity in our pipeline for investment, affecting an estimated 350 million people worldwide. We have identified several microRNA targets that serve as host factors for the virus. Our lead compound directed to one of the host microRNAs has demonstrated sub-nanomolar potency against HBV DNA replication and more than 95% reduction in Hepatitis B surface antigen in in vitro studies. We believe that targeting a host factor in the liver represents a unique mechanism of action for treatment of the virus compared to other programs in development and holds the potential for achieving a functional cure. We currently expect to submit an investigational new drug application ("IND") to the U.S. Food and Drug Administration ("FDA") for the HBV program in the second half of 2019, with the potential of achieving human proof-of-concept in a Phase 1 clinical trial.

Glioblastoma multiforme program: Our lead anti-miR candidate targeting microRNA-10b demonstrated statistically significant improvements in survival as both a monotherapy as well as in combination with temozolamide (TMZ) in an orthotopic glioblastoma multiforme animal model. In combination with TMZ, the addition of a single dose of anti-mir-10b, delivered intracranially, led to a more than two-fold improvement in survival compared to TMZ alone. These, and additional survival data on our lead anti-miR candidate, will be presented in November 2018 at the Society for Neuro-Oncology Meeting in New Orleans, Louisiana. We expect to nominate a clinical candidate by

year-end and plan to seek a partner to further advance its development.

Non-Alcoholic Steatohepatitis program: Across multiple animal models of NASH, our lead candidate has demonstrated improvement in key endpoints, including NAFLD Activity Score (NAS), liver transaminases, hyperglycemia, and disease-related gene expression. In the diet-induced NASH mouse model (Amylin model) after two to four weekly doses, early onset of improvement across multiple disease parameters including liver triglycerides and blood levels of transaminases was observed. After nine weeks of treatment, there was evidence of sustained benefit with significant improvement of liver fibrosis and hyperglycemia compared to control-treated animals. We believe that targeting dysregulated microRNA in a complex disease

like NASH may offer a unique mechanism of action from other programs in development. We plan to seek a partner to further advance its development.

FINANCIAL OPERATIONS OVERVIEW

Revenue

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

In the future, we may generate revenue from a combination of license fees and other upfront payments, payments for research and development services, milestone payments, product sales and royalties in connection with strategic alliances. We expect that any revenue we generate will fluctuate from quarter-to-quarter as a result of the timing of our achievement of preclinical, clinical, regulatory and commercialization milestones, if at all, the timing and amount of payments relating to such milestones and the extent to which any of our products are approved and successfully commercialized by us or our strategic alliance partners. If our current or future strategic alliance partners do not elect or otherwise agree to fund our development costs pursuant to our current or future strategic alliance agreement, or we or our strategic alliance partner fails 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 microRNAs with the goal of understanding how they function and identifying those that might be targets for therapeutic modulation. At any given time we are working on multiple targets, primarily within our therapeutic areas of focus. Our organization is structured to allow the rapid deployment and shifting of resources to focus on the best known targets based on our ongoing research. As a result, in the early phase of our development programs, our research and development costs are not tied to any specific target. However, we are currently spending the vast majority of our research and development resources on our lead development programs.

Since our inception, we have spent a total of approximately $340.4 million in research and development expenses through September 30, 2018.

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.

Successful development of future product candidates is highly uncertain and may not result in approved products. Completion dates and completion costs can vary significantly for each future product candidate and are difficult to predict. We anticipate we will make determinations as to which programs to pursue and how much funding to direct to each program on an ongoing basis in response to our ability to maintain or enter into new strategic alliances with

respect to each program or potential product candidate, the scientific and clinical success of each future product candidate, as well as ongoing assessments

as to each future product candidate's commercial potential. We will need to raise additional capital and may seek additional strategic alliances in the future in order to advance our various programs.

General and administrative expenses

General and administrative expenses consist primarily of salaries and related benefits, including stock-based compensation, related to our executive, finance, legal, business development and support functions. Other general and administrative expenses include allocated facility-related costs not otherwise included in research and development expenses and professional fees for auditing, tax and legal services, some of which are incurred as a result of being a publicly-traded company.

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 short-term investments, 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.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

There have been no significant changes to our critical accounting policies since December 31, 2017, with the exception of changes made upon adoption of ASU No. 2014-09 and the related supplemental ASUs. 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. For a description of accounting policy changes resulting from the adoption of ASU No. 2014-09 and the related supplemental ASUs, refer to 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, 2018 and 2017

The following table summarizes our results of operations for the three and nine months ended September 30, 2018 and 2017 (in thousands):

	Three months ended September 30,		Nine months ended September 30,	
	2018	2017	2018	2017
Revenue under strategic alliances and collaborations	$18	$ 18	$54	$ 54
Research and development expenses	6,879	12,697	28,720	42,727
General and administrative expenses	2,993	2,736	10,115	13,752
Interest and other expenses, net	(419)	(420)	(1,365)	(1,171)

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. Revenue under our strategic alliance was less than $0.1 million for each of the three and nine months ended September 30, 2018 and 2017. As of September 30, 2018, we had $0.1 million of deferred revenue, which consisted of payments received through our strategic alliance that have not yet been recognized in accordance with our revenue recognition policies.

Upon adoption of ASU No 2014-09 and the related supplemental ASUs, we reclassified $1.8 million of contract liabilities into accumulated deficit through the modified retrospective method of adoption.

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):

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	Three months ended September 30, 2018	% of total	Three months ended September 30, 2017	% of total	Increase (decrease) $	Increase (decrease) %
Research and development						
Personnel and internal expenses	$ 4,597	67 %	$ 4,526	36 %	$71	2 %
Third-party and outsourced expenses	1,541	22 %	7,030	55 %	(5,489)	(78)%
Non-cash stock-based compensation	522	8 %	653	5 %	(131)	(20)%
Depreciation	219	3 %	488	4 %	(269)	(55)%
Total research and development expenses	$ 6,879	100%	$ 12,697	100%	$(5,818)	(46)%

	Nine months ended September 30, 2018	% of total	Nine months ended September 30, 2017	% of total	Increase (decrease) $	Increase (decrease) %
Research and development						
Personnel and internal expenses	$ 13,340	47 %	$ 17,227	40 %	$(3,887)	(23)%
Third-party and outsourced expenses	12,932	45 %	22,857	54 %	(9,925)	(43)%
Non-cash stock-based compensation	1,776	6 %	1,012	2 %	764	75 %
Depreciation	672	2 %	1,631	4 %	(959)	(59)%
Total research and development expenses	$ 28,720	100%	$ 42,727	100%	$(14,007)	(33)%

Research and development expenses were $6.9 million and $28.7 million for the three and nine months ended September 30, 2018, respectively, compared to $12.7 million and $42.7 million for the three and nine ended September 30, 2017, respectively. The aggregate decreases were driven by a $5.5 million and $9.9 million decrease in external development expenses during the three and nine month periods ended September 30, 2018, respectively, primarily attributable to the pausing of the RG-012 and RGLS4326 programs early in the third quarter of 2018 and the discontinuation of the RG-101 and RGLS5040 programs in 2017. Additionally, the decrease for the nine months ended September 30, 2018 as compared to the nine months ended September 30, 2017 was driven by a $3.9 million reduction in personnel and internal expenses, primarily attributable to a reduction in costs subsequent to our corporate restructurings.

General and administrative expenses

General and administrative expenses were $3.0 million and $10.1 million for the three and nine months ended September 30, 2018, respectively, compared to $2.7 million and $13.8 million for the three and nine months ended September 30, 2017, respectively. The increase for the three months ended September 30, 2018 as compared to the three months ended September 30, 2017 was driven by non-recurring severance charges of $0.3 million recorded in the third quarter of 2018 in connection with our July 2018 corporate restructuring. The decrease for the nine months ended September 30, 2018 as compared to the nine months ended September 30, 2017 was driven by non-recurring severance charges of $1.0 million and non-recurring, non-cash stock-based compensation charges of $2.7 million recorded in connection with our May 2017 corporate restructuring.

Interest and other expenses, net

Net interest and other expenses were $0.4 million and $1.4 million for the three and nine months ended September 30, 2018, respectively, compared to $0.4 million and $1.2 million for the three and nine months ended September 30, 2017, respectively, primarily related to interest charges associated with our outstanding Term Loan.

LIQUIDITY AND CAPITAL RESOURCES

Since our inception through September 30, 2018, we have received $85.1 million from our strategic alliances and collaborations, principally from upfront payments, research funding and preclinical and clinical milestones, $300.1 million from the sale of our equity and convertible debt securities and $19.8 million in net proceeds from our Term Loan. As of September 30, 2018, we had cash, cash equivalents and short-term investments of $20.5 million.

The accompanying financial statements have been prepared on a basis which assumes we are a going concern, and does not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classifications of liabilities that may result from any uncertainty related to our ability to continue as a going concern.

If we are unable to maintain sufficient financial resources, our business, financial condition and results of operations will be materially and adversely affected. There can be no assurance that we will be able to obtain the needed financing on acceptable terms or at all. Additionally, equity or debt financings may have a dilutive effect on the holdings of the Company's existing stockholders. These factors raise substantial doubt about our ability to continue as a going concern.

Our future capital requirements are difficult to forecast and will depend on many factors, including:

- whether and when we achieve any milestones under our strategic alliance agreement with Sanofi;
- the terms and timing of any other strategic alliance, licensing and other arrangements that we may establish;
- the initiation, progress, timing and completion of preclinical studies and clinical trials for our development programs and product candidates, and associated costs;
- the number and characteristics of product candidates that we pursue;
- the outcome, timing and cost of regulatory approvals;
- delays that may be caused by changing regulatory requirements;
- the cost and timing of hiring new employees to support our continued growth;
- the costs involved in filing and prosecuting patent applications and enforcing and defending patent claims;
- the costs and timing of procuring clinical and commercial supplies of our product candidates;
- the costs and timing of establishing sales, marketing and distribution capabilities;
- the extent to which we acquire or invest in businesses, products or technologies; and
- payments under our Term Loan.

The following table shows a summary of our cash flows for the nine months ended September 30, 2018 and 2017 (in thousands):

	Nine months ended September 30,	
	2018	2017
	(unaudited)	
Net cash (used in) provided by:		
Operating activities	$(39,256)	$(47,672)
Investing activities	40,079	9,538
Financing activities	(258)	43,415
Total	$565	$5,281

Operating activities

Net cash used in operating activities was $39.3 million for the nine months ended September 30, 2018, compared to $47.7 million for the nine months ended September 30, 2017. The decrease in net cash used in operating activities was primarily attributable to a net loss of $40.1 million for the nine months ended September 30, 2018, compared to a net loss of $57.5 million for the nine months ended September 30, 2017. This decrease was partially offset by changes in working capital, resulting in a decrease in net cash used in operating activities of $5.4 million for the nine months ended September 30, 2018, compared to an increase in net cash used in operating activities of $0.8 million for the nine months ended September 30, 2017. Additionally, the decrease was partially offset by adjustments for non-cash charges, including stock-based compensation, resulting in decreases in net cash used in operating activities of $6.3 million for the nine months ended September 30, 2018, compared to decreases in net cash used in operating activities of $9.0 million for the nine months ended September 30, 2017.

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 $40.1 million for the nine months ended September 30, 2018, compared to $9.5 million for the nine months ended September 30, 2017.

Financing activities

Net cash used in financing activities was $0.3 million for the nine months ended September 30, 2018, compared to net cash provided by financing activities of $43.4 million for the nine months ended September 30, 2017. Net cash used in financing activities for the nine months ended September 30, 2018 was primarily attributable to the remittance of our first principal amortization payment due under our outstanding Term Loan, partially offset by proceeds from capital lease financing activities. Net cash provided by financing activities for the nine months ended September 30, 2017 was primarily attributable to $43.0 million in net proceeds received from our public offering in July 2017.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

As of September 30, 2018, there have been no material changes, outside of the ordinary course of business, in our outstanding contractual obligations from those disclosed within the contractual obligations table under “Management's Discussion and Analysis of Financial Condition and Results of Operations”, as contained in our Annual Report, other than the August 2018 amendment to our Loan Agreement (refer to Note 5 for information regarding our Loan Agreement).

Off-Balance Sheet Arrangements

As of September 30, 2018, 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 where a change in prevailing interest rates may cause the principal amount of short-term investments 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 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 short-term investments 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 short-term investments, we do not believe that an increase in market rates would have any significant impact on the realized value of our short-term investments. If a 10% change in interest rates were to have occurred on September 30, 2018, 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 Term Loan. As of September 30, 2018, the outstanding principal amount of the Term Loan was $19.2 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, 2018, 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 provide reasonable assurance 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

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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, 2018, 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, 2018.

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 February 17, 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. On December 22, 2017, lead plaintiffs filed a consolidated complaint against the Company, Dr. Grint, Mr. Hagan, and Michael Huang (our former Vice President of Clinical Development). The consolidated complaint alleges that between February 17, 2016 and June 12, 2017, the Defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, by making materially false and misleading statements regarding RG-101. The consolidated complaint seeks unspecified monetary damages and an award of attorneys' fees and costs. On February 6, 2018, defendants filed a Motion to Dismiss the Consolidated Complaint. On March 23, 2018, plaintiff filed their opposition to the motion and on April 24, 2018, defendants filed their response. No hearing date has been set. 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 will need to raise additional capital, and if we are unable to do so when needed, we will not be able to continue as a going concern. *

This Form 10-Q includes disclosures regarding management's assessment of our ability to continue as a going concern and our Annual Report on Form 10-K for the year ended December 31, 2017 includes a report from our independent registered public accounting firm that contains an explanatory paragraph regarding going concern, as our current liquidity position and recurring losses from operations since inception and negative cash flows from operating activities raise substantial doubt about our ability to continue as a going concern. As of September 30, 2018, we had $20.5 million of cash, cash equivalents and short-term investments and we had $19.2 million of outstanding debt principal obligations under our Term Loan with Oxford. In addition, pursuant to the terms of the Fourth Amendment, we are required to maintain cash in a collateral account controlled by the Lender of (i) $10.0 million if a Capital Event has not occured, or (ii) $5.0 million if a Capital Event has occurred. We will need to raise additional capital to fund our operations, service our debt obligations and comply with the cash reserve covenant under our Loan Agreement with Oxford, and if we are unable to raise additional capital when needed, we will not be able to continue as a going concern.

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 fund our operations and such funding may not be available to us on acceptable terms, or at all.

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. For example, in July 2018 we voluntarily paused our Phase I MAD clinical trial for RGLS4326 due to unexpected observations in our 27-week mouse chronic toxicity study, which was designed to support the Phase II proof-of-concept clinical trial in ADPKD previously planned to start in mid-2019. In consultation with the FDA, we initiated a new mouse chronic toxicity study in September 2018 with certain changes that are believed to address the unexpected observations. Additionally, our strategic alliance partners may not elect to pursue the development and commercialization of any of our microRNA product candidates that are subject to their respective strategic alliance agreements with us. Any of these events may increase our development costs more than we expect. For example, in June 2017, AstraZeneca terminated its development of RG-125(AZD4076). Upon the effective date of termination, in June 2019, 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. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi, which will be responsible for all costs incurred in the development of our miR-21 programs. As a result, we will not receive royalties in the event our miR-21 programs are eventually commercialized and will also receive significantly reduced milestones for these programs. 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.

For the foreseeable future, we expect to rely primarily on equity and/or debt financings to fund our operations. Raising additional capital through the sale of securities could cause significant dilution to our stockholders. Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates. Our ability to raise additional funds will depend, in part, on the success of our preclinical studies and clinical trials and other product development activities, regulatory events, our ability to identify and enter into licensing or other strategic arrangements, and other events or conditions that may

affect our value or prospects, as well as factors related to financial, economic and market conditions, many of which are beyond our control. There can be no assurances that sufficient funds will be available to us when required or on acceptable terms, 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, or amend existing alliances, for research and development programs at an earlier stage than otherwise would be desirable or for the development of programs that we otherwise would have sought to develop independently, or on terms that are less favorable than might otherwise be available;
- dispose of technology assets, 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;
- pursue the sale of our company to a third party at a price that may result in a loss on investment for our stockholders; or
- file for bankruptcy or cease operations altogether.

Any of these events could have a material adverse effect on our business, operating results and prospects.

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. *

Since inception, our operations have been primarily limited to acquiring and in-licensing intellectual property rights, developing our microRNA product platform, undertaking basic research around microRNA targets and conducting preclinical and clinical studies for our initial programs. We have 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 $10.3 million and $40.1 million for the three and nine months ended September 30, 2018, respectively, compared to $15.8 million and $57.5 million for the three and nine months ended September 30, 2017, respectively. As of September 30, 2018, we had an accumulated deficit of $384.2 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 Term Loan 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. Under our collaboration and license agreement with Sanofi, Sanofi has an option to obtain exclusive worldwide licenses for the development, manufacture and commercialization of our preclinical program targeting miR-221/222 for HCC. If Sanofi exercises its option, 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, 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. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi, which will be responsible for all costs incurred in the development of our miR-21 programs. 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 was to become effective in June 2018. In May 2018, AstraZeneca requested to extend the agreement termination effective date by an additional 12 months to allow AstraZeneca to complete all activities involving AZD4076. By the end of this 12-month extension, the parties will complete the transfer activities contemplated by the agreement. The new termination effective date pursuant to the extension will be June 2019.

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 initiated clinical development of RGLS4326 for the treatment of ADPKD. 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 microRNA targets and product candidates; acquire or in-license other products and technologies; continue with clinical development of our product candidates; seek marketing

approvals for our product candidates that successfully complete clinical trials; ultimately establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval; maintain, expand and protect our intellectual property portfolio; hire additional clinical, regulatory, research and administrative personnel; and create 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 microRNAs as therapeutic targets;
- completing our research and preclinical development of product candidates;
- initiating and completing clinical trials for product candidates;
- seeking and obtaining marketing approvals for product candidates that successfully complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties;
- launching and commercializing product candidates for which we obtain marketing approval, with an alliance partner or, if launched independently, successfully establishing a sales force, marketing and distribution infrastructure;
- maintaining, protecting and expanding our intellectual property portfolio; and
- attracting, hiring and retaining qualified personnel.

Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to predict the timing or amount of increased expenses and when we will be able to achieve or maintain profitability, if ever. In addition, our expenses could increase beyond expectations if we are required by the FDA or foreign regulatory agencies to perform studies and trials in addition to those that we currently anticipate.

Even if one or more of the product candidates that we independently develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

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 Loan of $20.0 million. Our obligations under the Loan Agreement are secured by a first priority security interest in substantially all of our current and future assets, except for the Assigned Assets that were licensed, assigned and transferred to Sanofi pursuant to the 2018 Sanofi Amendment, provided that the Oxford will continue to have liens on all proceeds received by us pursuant to the Sanofi License. We have also agreed not to encumber our intellectual property assets, except as permitted by the Loan Agreement. Amounts outstanding under the Term Loan mature on June 1, 2020 and were interest-only through June 1, 2018. On August 6, 2018, we and Oxford entered into an amendment to the parties' Loan Agreement. Under the terms of the amendment, we were required to make payments of interest-only for an additional three-month period, from August 2018 through October 2018. Amortization payments commence in November 2018. On November 5, 2018 and in connection with the 2018 Sanofi Amendment we entered into the Fourth Amendment with the Lender. Under the terms of the Fourth Amendment, we are required to prepay part of the Term Loan with 25% of certain payments we receive under the 2018 Sanofi Amendment, which payments consist of the Upfront Amendment Payments and the first development milestone payment in the amount of $10.0 million. We will also be required to pay the applicable 5.5% final payment fee related to each such 2018 Sanofi Amendment prepayment. In addition, we are required to maintain cash in a collateral account controlled by the Lender of (i) $10.0 million if a Capital Event has not occurred, or (ii) $5.0 million if a Capital Event has occurred. Payments under the Loan Agreement could result in a significant reduction of our assets.

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

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

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

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

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

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

- our research methodology or that of any strategic alliance partner 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 current or future 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.

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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 microRNAs. Our ability to generate product revenues, which we do not expect will occur for many years, if ever, will depend heavily on the successful development and eventual commercialization of our product candidates.

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

- 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.

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 a strategic alliance partner 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, which ultimately led to our identification of a bilirubin transport mechanism as the likely cause for the cases of SAEs of jaundice and our decision to discontinue clinical development of RG-101. In July 2018, we voluntarily paused our Phase I MAD clinical trial for RGLS4326 due to unexpected observations in our 27-week mouse chronic toxicity study, which was designed to support the Phase II proof-of-concept clinical trial in ADPKD previously planned to start in mid-2019. The observations in the mouse chronic toxicity study were unexpected, given the favorable safety profile of RGLS4326 in previous non-GLP and GLP toxicity studies at the same or similar doses supporting the IND and Phase I clinical trial. In consultation with the FDA, we initiated a new mouse chronic toxicity study with certain changes that are believed to address the unexpected observations.

If we or our current or future 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 moderately positive or if there are safety concerns, we or our current or future 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 a strategic alliance partner, 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 a strategic alliance partner may develop under an agreement with us, 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.

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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 on our own or with a strategic alliance partner.
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 any strategic alliance partner 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 a strategic alliance partner 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 microRNA 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 microRNA targets. Because our programs may involve a range of microRNA 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

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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, our existing strategy is to pursue 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, HCV, and HBV, 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.

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RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES

We will depend upon strategic alliances for the development and eventual commercialization of certain microRNA 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 strategic alliance partners for financial and scientific resources for the clinical development and commercialization of certain of our microRNA product candidates. These strategic alliances will likely provide us with limited control over the course of development of a microRNA 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 our preclinical program targeting miR-221/222 for HCC upon the achievement of relevant endpoints in clinical trials. However, Sanofi is not under any obligation to exercise this option. 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. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi, who will be responsible for all costs incurred in the development of our miR-21 program. As a result, we will not receive royalties in the event our miR-21 programs are eventually commercialized and will also receive significantly reduced milestones for these programs.

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 was to become effective in June 2018. In May 2018, AstraZeneca requested to extend the collaboration and license agreement termination effective date by an additional 12 months to allow AstraZeneca to complete all activities involving AZD4076. By the end of this 12-month extension, the parties will complete the transfer activities contemplated by the agreement. The new termination effective date

pursuant to the extension will be June 2019. 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 microRNA 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;

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- 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, in November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi, who will be responsible for all costs incurred in the development of our miR-21 programs. As a result, we will no longer be involved in the development or commercialization of our miR-21 programs. 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.

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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 microRNA therapeutics space, including patents and patent applications related to targeting microRNAs, 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 microRNA 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 microRNA therapeutics based on oligonucleotides that modulate microRNAs. 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.

In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program, to Sanofi, who will be responsible for all costs incurred in the development of our miR-21 programs. As a result, we will have no influence and/or control over their approaches to development and commercialization of our miR-21 programs. 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, and except in the case of RG-012, we have the right to assume the responsibility at our own expense for the development of the applicable microRNA 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 microRNA 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 microRNA product platform and future product candidates;
- obtain required regulatory approvals; and
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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 HCV 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-221/222 program, 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. *

If any 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. *

In early July 2018, we implemented a corporate restructuring which involved a reduction in our total workforce by approximately 60%. The workforce reduction was substantially completed in July 2018. As of September 30, 2018, we had 25 employees. In the future, we may need to expand our organization.

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 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 and in July 2018, each of which 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, additional reporting requirements and/or oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, 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.

For example, there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders designed to delay the implementation of any certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been signed into law. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". Additionally, on January 23, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. As a result, there is significant uncertainty regarding future healthcare reform and its impact on our operations.

Further, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed bills designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing,

including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, to encourage importation from other countries and bulk purchasing.

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.

Cybersecurity 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, 2015 through November 2, 2018, the closing price of our common stock as reported on The Nasdaq Global Market has ranged from $1.75 to $253.56, as adjusted for our 1-for-12 reverse stock split that became effective on October 3, 2018.

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.

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. 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. 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 have devoted and will need to continue 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.

Changes or modifications in financial accounting standards, including those related to revenue recognition, may harm our results of operations. *

From time to time, the Financial Accounting Standards Board, or FASB, either alone or jointly with other organizations, promulgates new accounting principles that could have an adverse impact on our financial position, results of operations or reported cash flows. In May 2014, the FASB issued Accounting Standards Update, or ASU, No. 2014-09, Revenue from Contracts with Customers (Topic 606), which requires an entity to recognize the amount of revenue when promised goods or services are transferred to customers. The standard requires a company to recognize revenue to depict the transfer of goods or services to customers in the amount that reflects the consideration it expects to be entitled to receive in exchange for those goods or services. The FASB subsequently issued amendments to ASU No. 2014-09 that have the same effective date and transition date. These new standards became effective for us on January 1, 2018 and were adopted using the modified retrospective method through a cumulative-effect adjustment directly to accumulated deficit of $1.8 million.

Any difficulties in adopting or implementing any new accounting standard could result in our failure to meet our financial reporting obligations, which could result in regulatory discipline and harm investors' confidence in us. Finally, if we were to change our critical accounting estimates, including those related to the recognition of collaboration revenue, our operating results could be significantly affected.

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.

Substantially all of our outstanding shares of common stock are available for public sale, subject in some cases to volume and other limitations. If our existing stockholders sell substantial amounts of our common stock in the public market, or the market perceives that such sales may occur, 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.

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. In addition, if eligible optionholders choose not to participate in the Exchange Offer, our employees and directors who hold such options may not be properly incentivized.*

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, preferred 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 (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 ("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 in 2015 (the "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.

On October 15, 2018, we commenced the Exchange Offer pursuant to which certain eligible optionholders, subject to specified conditions, will be able exchange some or all of their outstanding options to purchase shares of our common stock for new RSUs. Shares of our common stock underlying eligible options granted under our 2009 Equity Incentive Plan or the 2012 Plan that are properly exchanged in the Exchange Offer will return to our 2012 Plan and become available for issuance under new stock award grants under our 2012 Plan, including the new RSUs. Shares of our common stock underlying eligible options granted under the Inducement Plan that are properly exchanged in the Exchange Offer will not become available for grant under the 2012 Plan or otherwise.

The purpose of the Exchange Offer is to revitalize the incentive value of our outstanding equity awards to retain and motivate employees and directors and recreate a personal stake in the long term financial success of our company, and thereby align their interests with those of our other stockholders. Equity awards are a critical component of our compensation philosophy, the focal point of which is to increase long-term stockholder value. During the past several fiscal years, our stock price has declined. As of October 15, 2018, 100% of our outstanding stock options were "underwater," meaning the exercise price of each of those options is greater than our current stock price, with exercise prices ranging from $4.56 to over $200 per share; a significant portion of these options have been "underwater" for more than two years. Specifically, all stock options granted between February 2012 and October 2016 have been "underwater" in their entirety for more than two years. This means that our historically granted stock options may have little or no perceived value to those who hold them and therefore may no longer be effective as incentives to motivate and retain these individuals. If eligible optionholders choose not to participate in the Exchange Offer, our employees and directors who hold such options may not be properly incentivized.

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. For example, in December 2017, we received a letter from The Nasdaq Stock Market advising us that for 30 consecutive trading days preceding the date of the letter, the bid price of our common stock had closed below the $1.00 per share minimum required for continued listing on The Nasdaq Global Market, and therefore we could become subject to delisting if we did not regain compliance within the compliance period. In January 2018, we were notified by The Nasdaq Stock Market that for a period of 10 consecutive trading days, we had maintained a closing bid above $1.00 and therefore had regained compliance with Nasdaq listing rules. In April 2018, we again received a letter from The Nasdaq Stock Market advising us that for 30 consecutive trading days preceding the date of the letter, the bid price of our common stock had closed below the $1.00 per share minimum price required for continued listing on The Nasdaq Global Market, and therefore we could become subject to delisting if our common stock does not meet the $1.00 minimum bid price for 10 consecutive trading days within the 180-day period following the date of the letter. On October 2, 2018 we filed a Certificate of Amendment of Amended and Restated Certificate of Incorporation with the Secretary of State of the state of Delaware to effect a 1-for-12 reverse stock split of our issued and outstanding common stock. The reverse stock split became effective at 5:00 p.m. Eastern Time on October 3, 2018 and our shares of common stock began trading on a split-adjusted basis on The Nasdaq Global Market on October 4, 2018. On October 18, 2018, we were notified by The Nasdaq Stock Market that as of October 17, 2018 we had maintained a closing bid above $1.00 for a period of 10 consecutive trading days

and therefore had regained compliance with Nasdaq listing rules. There can be no assurance that we will continue to be in compliance with the $1.00 minimum bid price requirement or comply with Nasdaq's other continued listing standards in the future. If in the future we are not able to regain compliance with the minimum bid price requirement within the allotted 180-day period, 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. In addition, the delisting of our common stock from The Nasdaq Global Market would constitute an event of default under our Loan Agreement with Oxford.

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. These actions were consolidated and on December 22, 2017, lead plaintiffs filed a consolidated complaint against the Company, Dr. Grint, Mr. Hagan, and Michael Huang (our former Vice President of Clinical Development). The consolidated complaint alleges that between February 17, 2016 and June 12, 2017, the Defendants violated Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, by making materially false and misleading statements regarding RG-101. The consolidated complaint seeks unspecified monetary damages and an award of attorneys' fees and costs. On February 6, 2018, defendants filed a Motion to Dismiss the consolidated complaint. On March 23, 2018, plaintiff filed their opposition to the motion and on April 24, 2018, defendants filed their response. No hearing date has been set. We are not able to predict or reasonably estimate the ultimate outcome or possible losses relating to these claims. 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. 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.

As of December 31, 2017, we had federal and state net operating loss carryforwards of $265.8 million and $146.3 million, respectively. The federal and state net operating loss carryforwards will begin to expire, if not utilized, in 2030 and 2031. These net operating loss carryforwards could expire unused and be unavailable to offset future income tax liabilities. Under the newly enacted federal income tax law, federal net operating losses incurred in 2018 and in future years may be carried forward indefinitely, but the deductibility of such federal net operating losses is limited. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law. In addition, under Section 382 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is 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 some of which may be outside of our control. As a result, if we earn net taxable income, our ability to use our pre-ownership 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

First Amendment to Second Amended and Restated Collaboration and License Agreement

On November 5, 2018, we entered into the 2018 Sanofi Amendment with Sanofi to modify the parties' rights and obligations with respect to our miR-21 programs, including our RG-012 program.

Under the terms of the 2018 Sanofi Amendment, we have granted Sanofi a worldwide, royalty-free, fee-bearing, exclusive license, with the right to grant sublicenses, under our know-how and patents to develop and commercialize miR-21 compounds and products for all indications, including Alport Syndrome. Sanofi will control and will assume all responsibilities and obligations for developing and commercializing each of our miR-21 programs, including our obligations regarding the administration and expense of clinical trials and all other costs, including in-license royalties and other in-license payments, related to our miR-21 programs. Under the terms of the 2018 Sanofi Amendment, we have assigned to Sanofi certain agreements and all materials directed to miR-21 or to any miR-21 compound or product and are required to provide reasonable technical assistance to Sanofi for a period of 24 months after the date of the 2018 Sanofi Amendment.

Under the terms of the 2018 Sanofi Amendment, we are eligible to receive the Upfront Amendment Payments. We are also eligible to receive up to $40.0 million in development milestone payments. In addition, Sanofi has agreed to reimburse us for certain out-of-pocket transition activities and assume our upstream license royalty obligations. We and Sanofi also agreed to a general release of claims against each other for any claims that arose at any time prior to

the date of the 2018 Sanofi Amendment, or that thereafter could arise based on anything that occurred prior to the date of the 2018 Sanofi Amendment.

Fourth Amendment to Loan and Security Agreement

On November 5, 2018 and in connection with the 2018 Sanofi Amendment we entered into the Fourth Amendment with the Lender. Under the terms of the Fourth Amendment, the Lender has consented to the 2018 Sanofi Amendment and our license, assignment and transfer to Sanofi of the Assigned Assets, which previously served as collateral under the loan and

security agreement, and has released its liens in the Assigned Assets, provided that the Lender will continue to have liens on all proceeds received by us pursuant to the Sanofi License. Under the terms of the Fourth Amendment, we now have the option to prepay part of the Term Loan at any time and in any amount after 10 days' prior written notice. We are also required to prepay part of the Term Loan with 25% of certain payments we receive under the 2018 Sanofi Amendment, which payments consist of the Upfront Amendment Payments and the first development milestone payment in the amount of $10.0 million. We will be required to pay the applicable 5.5% final payment fee related to each such 2018 Sanofi Amendment prepayment. Under the Fourth Amendment, we are required to maintain cash in a collateral account controlled by the Lender of (i) $10.0 million if a Capital Event has not occurred, or (ii) $5.0 million if a Capital Event has occurred.

The maturity date of the Term Loan remains unchanged and the Term Loan is required to be paid in full on June 1, 2020.

The foregoing is only a summary of the material terms of the 2018 Sanofi Amendment and the Fourth Amendment, does not purport to be complete and is qualified in its entirety by reference to the full text of such amendments, which will be filed as exhibits to our Annual Report on Form 10-K for the fiscal year ending December 31, 2018.

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 (File No. 001-35670), filed with the SEC on August 3, 2016).
3.2	Certificate of Amendment of Amended and Restated Certificate of Incorporation of Regulus Therapeutics Inc. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (file No. 001-35670), filed with the SEC on October 2, 2018).
3.3	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on June 8, 2016).
4.1	Reference is made to Exhibits 3.1, 3.2 and 3.3.
4.2	Form of common stock certificate of the Registrant.
10.1†	Third Amendment to Loan and Security Agreement, dated August 6, 2018, by and between the Registrant and Oxford Finance LLC.
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.

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

* Indicates management contract or compensatory plan.

** 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 8, 2018 By: /s/ Joseph P. Hagan
Joseph P. Hagan
President and Chief Executive Officer
(Principal Executive Officer)

Date: November 8, 2018 By: /s/ Daniel R. Chevallard
Daniel R. Chevallard
Chief Financial Officer
(Principal Financial and Accounting Officer)