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

FORM 10-Q

(Mark One)

QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE QUARTERLY PERIOD ENDED JUNE 30, 2021

or

TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934
FOR THE TRANSITION PERIOD FROM _____ TO _____

Commission file number: 001-35670

Regulus Therapeutics Inc.
(Exact name of registrant as specified in its charter)

Delaware
(State or Other Jurisdiction of
Incorporation or Organization)

26-4738379
(I.R.S. Employer
Identification No.)

4224 Campus Point Court, Suite 210
San Diego
CA
(Address of Principal Executive Offices)

92121

(Zip Code)

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

(Former name, former address and former fiscal year, if changed since last report)

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	Trading Symbol(s)	Name of Each Exchange on Which Registered
Common Stock, par value \$0.001 per share	RGLS	The Nasdaq Stock Market LLC

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

Indicate by check mark whether the registrant has submitted electronically 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 such files). Yes No

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

Large accelerated filer
Non-accelerated filer

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

As of August 6, 2021, the registrant had 87,040,335 shares of Common Stock (\$0.001 par value) outstanding.

REGULUS THERAPEUTICS INC.
TABLE OF CONTENTS

PART I. FINANCIAL INFORMATION

Item 1. Financial Statements	3
Condensed Balance Sheets as of June 30, 2021 (Unaudited) and December 31, 2020	3
Condensed Statements of Operations and Comprehensive Loss for the three and six months ended June 30, 2021 and 2020 (Unaudited)	5
Condensed Statements of Changes in Stockholders' Equity (Deficit) for the three and six months ended June 30, 2021 and 2020 (Unaudited)	6
Condensed Statements of Cash Flows for the six months ended June 30, 2021 and 2020 (Unaudited)	8
Notes to Condensed Financial Statements (Unaudited)	9
Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations	21
Item 3. Quantitative and Qualitative Disclosures about Market Risk	29
Item 4. Controls and Procedures	29

PART II. OTHER INFORMATION

Item 1. Legal Proceedings	30
Item 1A. Risk Factors	30
Item 2. Unregistered Sales of Equity Securities and Use of Proceeds	59
Item 3. Defaults Upon Senior Securities	59
Item 4. Mine Safety Disclosures	59
Item 5. Other Information	59
Item 6. Exhibits	60

RISK FACTOR SUMMARY

Below is a summary of the material factors that make an investment in our common stock speculative or risky. This summary does not address all of the risks that we face. Additional discussion of the risks summarized in this risk factor summary, and other risks that we face, can be found below under the heading "Risk Factors" under Part II, Item 1A of this Quarterly Report and should be carefully considered, together with other information in this Quarterly Report before making investment decisions regarding our common stock.

- The approach we are taking to discover and develop drugs is novel and may never lead to marketable products.
 - We may not be successful in our efforts to identify or discover potential product candidates.
 - Preclinical and clinical studies of our product candidates may not be successful. If we are unable to generate successful results from our preclinical and clinical studies of our product candidates, or experience significant delays in doing so, our business may be materially harmed.
 - 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.
 - 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.
-

- 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.
 - 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.
 - 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.
 - We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.
 - We have never generated any revenue from product sales and may never be profitable.
 - We will depend upon collaborations for the development and eventual commercialization of certain *microRNA* product candidates. If these collaborations 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 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.
 - Manufacturing issues may arise that could increase product and regulatory approval costs or delay commercialization.
 - 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.
 - 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 face significant competition from other biotechnology and pharmaceutical companies and our operating results will suffer if we fail to compete effectively.
 - Our business could be adversely affected by the effects of health pandemics or epidemics, including the ongoing COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations, or materially affect our operations globally, including at our headquarters in San Diego, and at our clinical trial sites, as well as the business or operations of our collaborators, manufacturers, contract research organizations ("CROs") or other third parties with whom we conduct business.
 - The market price of our common stock may be highly volatile.
 - We may be unable to comply with the applicable continued listing requirements of The Nasdaq Capital Market.
-

PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

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

	June 30, 2021 (Unaudited)	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	\$ 41,440	\$ 31,087
Restricted cash	62	—
Contract and other receivables	194	503
Prepaid materials, net	3,269	3,314
Prepaid expenses and other current assets	1,348	1,826
Total current assets	46,313	36,730
Property and equipment, net	284	472
Intangibles, net	105	125
Right of use asset	2,814	253
Other assets	—	24
Total assets	\$ 49,516	\$ 37,604
Liabilities and stockholders' equity (deficit)		
Current liabilities:		
Accounts payable	\$ 1,393	\$ 535
Accrued liabilities	477	581
Accrued research and development expenses	762	1,097
Accrued compensation	1,158	1,743
Current portion of term loan, less debt issuance costs	4,662	4,652
Other current liabilities	1,516	2,970
Total current liabilities	9,968	11,578
Lease liability, less current portion	2,720	—
Total liabilities	12,688	11,578
Commitments and Contingencies	—	—
Stockholders' equity:		
Class A-1 convertible preferred stock, \$0.001 par value; 256,700 shares authorized, issued, and outstanding at June 30, 2021 (unaudited) and December 31, 2020	—	—
Class A-2 convertible preferred stock, \$0.001 par value; 1,330,832 and 1,416,453 shares authorized, issued, and outstanding at June 30, 2021 (unaudited) and December 31, 2020, respectively	1	1
Class A-3 convertible preferred stock, \$0.001 par value; 258,707 shares authorized, issued, and outstanding at June 30, 2021 (unaudited) and December 31, 2020	1	1
Common stock, \$0.001 par value; 400,000,000 shares and 200,000,000 authorized at June 30, 2021 and December 31, 2020, respectively; 87,040,335 and 67,432,712 shares issued and outstanding at June 30, 2021 (unaudited) and December 31, 2020, respectively	87	67
Additional paid-in capital	475,831	453,002
Accumulated deficit	(439,092)	(427,045)
Total stockholders' equity	36,828	26,026
Total liabilities and stockholders' equity	\$ 49,516	\$ 37,604

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 June 30,		Six months ended June 30,	
	2021	2020	2021	2020
	(Unaudited)			
Revenues:				
Revenue under collaborations	\$ —	\$ —	\$ —	\$ 6
Total revenues	—	—	—	6
Operating expenses:				
Research and development	4,150	4,242	7,470	7,360
General and administrative	2,488	2,254	4,967	4,676
Total operating expenses	6,638	6,496	12,437	12,036
Loss from operations	(6,638)	(6,496)	(12,437)	(12,030)
Other income (expense):				
Interest and other income	821	10	822	89
Interest and other expense	(216)	(461)	(431)	(951)
Loss before income taxes	(6,033)	(6,947)	(12,046)	(12,892)
Income tax (expense) benefit	(1)	—	(1)	8
Net loss and comprehensive loss	<u>\$ (6,034)</u>	<u>\$ (6,947)</u>	<u>\$ (12,047)</u>	<u>\$ (12,884)</u>
Net loss per share, basic and diluted	<u>\$ (0.08)</u>	<u>\$ (0.23)</u>	<u>\$ (0.16)</u>	<u>\$ (0.48)</u>
Weighted average shares used to compute basic and diluted net loss per share	<u>77,175,831</u>	<u>29,801,974</u>	<u>74,249,631</u>	<u>26,933,173</u>

See accompanying notes to these condensed financial statements.

Regulus Therapeutics Inc.
CONDENSED STATEMENTS OF CHANGES IN STOCKHOLDERS' EQUITY (DEFICIT)
(In thousands, except share data)

	Convertible preferred stock		Common stock		Additional paid-in capital	Accumulated deficit	Total stockholders' equity (deficit)
	Shares	Amount	Shares	Amount			
Balance at December 31, 2020	1,931,860	\$ 2	67,432,712	\$ 67	\$ 453,002	\$ (427,045)	\$ 26,026
Issuance of common stock upon vesting of restricted stock units	—	—	16,902	—	—	—	—
Issuance of common stock upon exercise of options	—	—	26,770	—	26	—	26
Issuance of common stock upon exercise of warrants	—	—	2,418,681	3	663	—	666
Issuance of common stock through ATM	—	—	4,009,585	4	5,709	—	5,713
Issuance of common stock under Employee Stock Purchase Plan	—	—	4,122	—	2	—	2
Conversions of convertible preferred stock	(78,036)	—	780,360	1	(1)	—	—
Stock-based compensation expense	—	—	—	—	691	—	691
Net loss	—	—	—	—	—	(6,013)	(6,013)
Balance at March 31, 2021	1,853,824	\$ 2	74,689,132	\$ 75	\$ 460,092	\$ (433,058)	\$ 27,111
Issuance of common stock upon vesting of restricted stock units	—	—	16,849	—	—	—	—
Issuance of common stock upon exercise of options	—	—	958	—	—	—	—
Issuance of common stock upon exercise of warrants	—	—	250,000	—	166	—	166
Issuance of common stock through ATM	—	—	12,007,546	12	14,819	—	14,831
Conversions of convertible preferred stock	(7,585)	—	75,850	—	—	—	—
Stock-based compensation expense	—	—	—	—	754	—	754
Net loss	—	—	—	—	—	(6,034)	(6,034)
Balance at June 30, 2021	1,846,239	\$ 2	87,040,335	\$ 87	\$ 475,831	\$ (439,092)	\$ 36,828
Balance at December 31, 2019	3,704,288	\$ 4	21,018,663	\$ 21	\$ 431,305	\$ (411,315)	\$ 20,015
Issuance of common stock upon vesting of restricted stock units	—	—	21,166	—	—	—	—
Issuance of common stock upon exercise of options	—	—	468	—	—	—	—
Issuance of common stock under Employee Stock Purchase Plan	—	—	1,666	—	1	—	1
Conversions of convertible preferred stock	(656,682)	(1)	6,566,820	7	(6)	—	—
Stock-based compensation expense	—	—	—	—	823	—	823
Net loss	—	—	—	—	—	(5,937)	(5,937)
Balance at March 31, 2020	3,047,606	\$ 3	27,608,783	\$ 28	\$ 432,123	\$ (417,252)	\$ 14,902
Stock-based compensation expense	—	—	—	—	629	—	629
Issuance of common stock upon vesting of restricted stock units	—	—	17,703	—	—	—	—
Conversions of convertible preferred stock	(829,643)	(1)	8,296,430	8	(7)	—	—
Net loss	—	—	—	—	—	(6,947)	(6,947)
Balance at June 30, 2020	2,217,963	\$ 2	35,922,916	\$ 36	\$ 432,745	\$ (424,199)	\$ 8,584

See accompanying notes to these condensed financial statements.

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

	Six months ended June 30,	
	2021	2020
	(Unaudited)	
Operating activities		
Net loss	\$ (12,047)	\$ (12,884)
Adjustments to reconcile net loss to net cash used in operating activities		
Depreciation and amortization expense	380	248
Stock-based compensation	1,445	1,452
Gain on PPP Loan forgiveness	(662)	—
Other	22	143
Change in operating assets and liabilities:		
Contracts and other receivables	309	467
Prepaid materials	45	—
Prepaid expenses and other assets	501	647
Accounts payable	858	(297)
Accrued liabilities	(105)	(74)
Accrued research and development expenses	(335)	239
Accrued compensation	(585)	(738)
Operating lease right-of-use assets and liabilities, net	275	(72)
Contract liabilities	—	(6)
Other liabilities	(836)	(353)
Net cash used in operating activities	<u>(10,735)</u>	<u>(11,228)</u>
Investing activities		
Purchases of property and equipment	(184)	—
Net cash used in investing activities	<u>(184)</u>	<u>—</u>
Financing activities		
Proceeds from borrowing under Paycheck Protection Program	—	662
Proceeds from issuance of common stock, net	21,379	1
Proceeds from exercise of common stock options	27	—
Other	—	—
Payments on financing leases	(72)	(137)
Net cash provided by financing activities	<u>21,334</u>	<u>526</u>
Net increase (decrease) in cash and cash equivalents	10,415	(10,702)
Cash and cash equivalents at beginning of period	31,087	34,121
Cash and cash equivalents at end of period	<u>\$ 41,502</u>	<u>\$ 23,419</u>
Reconciliation of cash, cash equivalents and restricted cash		
Cash and cash equivalents	\$ 41,440	\$ 23,419
Restricted cash	62	—
Total cash, cash equivalents and restricted cash	<u>\$ 41,502</u>	<u>\$ 23,419</u>
Supplemental disclosure of cash flow information		
Paycheck Protection Program loan forgiveness	<u>\$ 662</u>	<u>\$ —</u>
Interest paid	<u>\$ (222)</u>	<u>\$ (728)</u>
Income taxes (paid) refunded	<u>\$ (1)</u>	<u>\$ 8</u>

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, 2020, from which the balance sheet information herein was derived.

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, totaling \$505.6 million. As of June 30, 2021, we had approximately \$41.4 million of cash and cash equivalents. Based on our operating plans, we believe our cash and cash equivalents 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 June 30, 2021 and December 31, 2020, due to the considerations discussed above and the assessment that the material adverse change clause under the Term Loan is not within our control. In the first quarter of 2021, we received a waiver from the Lender (as defined below) with respect to noncompliance with a covenant under the Loan Agreement (as defined below). We are in compliance with all Loan Agreement covenants.

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. Additionally, the impact of the COVID-19 pandemic to our business and operating results presents additional uncertainty.

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 license and collaboration agreements.

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 could 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 and 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 preclinical and 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 an impairment is identified.

Recent Accounting Pronouncements

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*. Subsequently, in November 2018, the FASB issued ASU 2018-19, *Codification Improvements to Topic 326, Financial Instruments-Credit Losses*. ASU 2016-13 requires entities to measure all expected credit losses for most financial assets held at the reporting date based on an expected loss model which includes historical experience, current conditions, and reasonable and supportable forecasts. ASU 2016-13 also requires enhanced disclosures to help financial statement users better understand significant estimates and judgments used in estimating credit losses. This ASU is effective for smaller reporting companies for fiscal years beginning after December 15, 2022, with early adoption permitted. We are assessing the impact this standard will have on our financial statements and disclosures.

In March 2020, the FASB issued ASU No. 2020-04, *Reference Rate Reform (Topic 848)*, which provides guidance around reference rate reform initiatives to identify alternative reference rates that are more observable or transaction-based and less susceptible to manipulation in response to concerns about structural risks of interbank offered rates and the risk of cessation of the London Interbank Offered Rate ("LIBOR"). The amendments in the ASU provide option expedients and exceptions for applying GAAP to contracts, hedging relationships and other transactions affected by reference rate reform and apply only if such contracts, hedging relationships and other transactions that reference LIBOR or another reference rate are expected to be discontinued because of reference rate reform. The guidance does not apply to contract modifications made, and hedging relationships entered into or evaluated, after December 31, 2022. We are assessing the impact this standard will have on our financial statements and disclosures.

In August 2020, the FASB issued ASU 2020-06, *Debt—Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging—Contracts in Entity’s Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity’s Own Equity*, which simplifies accounting for convertible instruments by removing major separation models required under current GAAP. This standard removes certain settlement conditions that are required for equity contracts to qualify for the derivative scope exception and it also simplifies the diluted earnings per share calculation in certain areas. This standard is effective for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. Early adoption is permitted, but no earlier than fiscal years beginning after December 15, 2020 and adoption must be as of the beginning of the Company’s annual fiscal year. The adoption of this standard on January 1, 2021 did not impact our financial statements or disclosures.

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 or if-converted method. Dilutive common stock equivalents are comprised of stock options, restricted stock units and convertible preferred stock outstanding. 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 common share, because to do so would be anti-dilutive, were (in common stock equivalent shares) 28,465,276 for the three months and six months ended June 30, 2021, consisting of convertible preferred stock, stock options and restricted stock units, and 28,577,380 for the three and six months ended June 30, 2020, consisting of convertible preferred stock, stock options and restricted stock units.

3. Investments

Historically, we have invested 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. As of June 30, 2021 and December 31, 2020, our cash balance was comprised entirely of cash and cash equivalents (money market funds).

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 June 30, 2021 and December 31, 2020 (in thousands):

	Fair value as of June 30, 2021			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents (money market funds)	\$ 36,903	\$ 36,903	\$ —	\$ —
	<u>\$ 36,903</u>	<u>\$ 36,903</u>	<u>\$ —</u>	<u>\$ —</u>

	Fair value as of December 31, 2020			
	Total	Level 1	Level 2	Level 3
Assets:				
Cash equivalents (money market funds)	\$ 26,901	\$ 26,901	\$ —	\$ —
	<u>\$ 26,901</u>	<u>\$ 26,901</u>	<u>\$ —</u>	<u>\$ —</u>

We obtain pricing information from quoted market prices or quotes from brokers/dealers. We have historically determined the fair value of our investment securities using standard observable inputs, including reported trades, broker/dealer quotes, bids and/or offers.

5. Debt

Term Loan

On June 17, 2016, we entered into a loan and security agreement ("Loan Agreement") with Oxford Finance, LLC, (the "Lender"), pursuant to which we received \$20.0 million in proceeds, net of debt issuance costs, on June 22, 2016 (the "Term Loan").

The outstanding Term Loan will mature on May 1, 2022 (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.

The Loan Agreement was amended eight times between October 2017 through May 2019. On May 1, 2020 we entered into a ninth amendment to the Term Loan with the Lender (the "Ninth Amendment"). Pursuant to the terms of the Ninth Amendment, (i) the approximately \$0.7 million of loan proceeds (the "PPP Loan") we received under the Paycheck Protection Program ("PPP") was included as permitted indebtedness under the terms of the Term Loan, (ii) we agreed to apply for forgiveness of the maximum amount of PPP Loan permissible in accordance with the Coronavirus Aid, Relief, and Economic Security Act (the "CARES Act") and use best efforts to cause not less than \$0.5 million of the PPP Loan to be forgiven by the PPP Loan lender on or before September 30, 2020 and (iii) we agreed not to amend any material provision in any document relating to the PPP Loan nor make any prepayment of the PPP Loan unless such prepayment is necessary or advisable due to change in the applicable law or guidance issued by the U.S. Small Business Administration ("SBA").

On August 25, 2020 we entered into a tenth amendment to the Term Loan with the Lender (the "Tenth Amendment"). Pursuant to the terms of the Tenth Amendment, we are eligible for up to an additional seven months of interest only payments in the event we paid down \$10.0 million in loan principal before April 30, 2021 (the "Principal Paydown Event"). In the event the Principal Paydown Event did not occur by April 30, 2021, we would make principal and accrued interest payments, in arrears, commencing May 1, 2021, in accordance with the terms of the Eighth Amendment. If the Principal Paydown Event occurred after April 30, 2021 but on or before July 31, 2021, we would recommence an extended interest only payment period through December 31, 2021. In the event we received the additional interest only period, principal and accrued interest payments would recommence on January 1, 2022.

We received \$1.0 million, \$4.0 million and \$5.0 million in proceeds from Sanofi (see Note 7) on September 30, 2020, October 8, 2020 and November 30, 2020, respectively. Under the terms of the Tenth Amendment, we prepaid \$1.0 million, \$4.0 million and \$5.0 million of outstanding principal to the Lender on September 30, 2020, October 8, 2020 and November 30, 2020, respectively, for a total of \$10.0 million. We also paid the applicable 5.5% final payment fees related to the three prepayments to the Lender. As the Principal Paydown Event occurred by April 30, 2021, we received an additional seven

months of interest only payment extension and are not obligated to make principal payments on the Term Loan until January 1, 2022.

We used 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, for which the Lender currently has a positive lien, and certain assets under finance 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. During the first quarter of 2021, we received a waiver from the Lender with respect to noncompliance with a covenant under the Loan Agreement. As of the date of the filing of this Form 10-Q, we are in compliance with all Loan Agreement covenants as of the date of the filing of this Form 10-Q.

As of June 30, 2021, \$4.7 million was outstanding under the Term Loan. An additional \$1.3 million is also payable at the conclusion of the Term Loan (presented in other current liabilities on our balance sheet at June 30, 2021). We had less than \$0.1 million of debt issuance costs outstanding as of June 30, 2021, which are being accreted to interest expense over the life of the Term Loan using an effective interest rate of 8.98%. The exit fees are being accrued over the life of the Term Loan through interest expense.

As of June 30, 2021, future principal payments for the Term Loan due under the Loan Agreement are as follows (in thousands):

2021	—
2022	4,681
	<u>\$ 4,681</u>

Paycheck Protection Program Loan

On April 23, 2020, we received the proceeds from the PPP Loan in the amount of approximately \$0.7 million from Silicon Valley Bank, as lender, pursuant to the PPP of the CARES Act. The PPP Loan was set to mature on April 23, 2022 and bore interest at a rate of 1.0% per annum. The PPP Loan was evidenced by a promissory note dated April 23, 2020, which contained customary events of default relating to, among other things, payment defaults and breaches of representations and warranties. The PPP Loan was prepayable by us at any time prior to maturity with no prepayment penalties.

Under the CARES Act and PPP Flexibility Act, loan forgiveness is available for the sum of documented payroll costs, covered mortgage interest, covered rent payments and covered utilities during the 24 week period beginning on the date of loan disbursement. For purposes of the PPP, payroll costs exclude compensation of an individual employee in excess of \$100,000, annualized, prorated for the covered period. Not more than 40% of the forgiven amount may be for non-payroll costs. Forgiveness is reduced if full-time headcount declines during the covered period as compared to specified reference periods, or if salaries and wages for employees with salaries of \$100,000 or less annually are reduced by more than 25%, unless certain safe harbors are satisfied. In the event the PPP Loan, or any portion thereof, is forgiven pursuant to the PPP, the amount forgiven is applied to outstanding principal and includes accrued interest.

We have used all proceeds from the PPP Loan to retain employees, maintain payroll and make lease and utility payments, and we sought forgiveness in accordance with the program. We received full forgiveness of our PPP Loan in the second quarter of 2021. We accounted for the full forgiveness of our PPP Loan by recording a gain in interest and other income for the three and six months ended June 30, 2021.

6. Stockholders' Equity

Common Stock

As of June 30, 2021, there were 87,040,335 shares of common stock outstanding. Each share of common stock is entitled to one vote. The holders of the common stock are also entitled to receive dividends whenever funds are legally available and when declared by our Board of Directors.

2019 Equity Incentive Plan

On June 15, 2019, the Company's board of directors approved, and on August 1, 2019 the Company's stockholders approved, the Company's 2019 Equity Incentive Plan (the "2019 Plan"). The 2019 Plan is intended as the successor to and continuation of the Company's 2012 Equity Incentive Plan. The number of shares authorized for issuance under the 2019 Plan may be increased by (a) the shares subject to outstanding stock awards granted under the Company's 2009 Equity Incentive Plan (the "2009 Plan") and the Company's 2012 Equity Incentive Plan (together with the 2009 Plan, the "Prior Plans") that on or after the effective date of the 2019 Plan (i) expire or terminate for any reason prior to exercise or settlement; (ii) are forfeited because of the failure to meet a contingency or condition required to vest such shares or otherwise return to the Company, or (iii) are reacquired, withheld (or not issued) to satisfy a tax withholding obligation in connection with an award or to satisfy the purchase price or exercise price of a stock award. No further grants will be made under the Prior Plans. In addition, on January 22, 2020, an additional 4,166,860 shares of common stock became available for issuance under the 2019 Plan pursuant to the Milestone Closing (defined below) of the May 2019 SPA (defined below). Further, on January 1st of each year, for a period of not more than ten years, beginning on January 1, 2021 and continuing through January 1, 2029, the number of shares authorized for issuance under the 2019 Plan will increase by 5.0% of the total number of shares of our capital stock outstanding on December 31 of the preceding calendar year, or a lesser number of shares as may be determined by our Board of Directors. As of June 30, 2021, 1,023,111 shares of common stock were available for new equity award grants under the 2019 Plan and 10,002,886 shares of common stock are reserved for issuance pursuant to equity awards outstanding as of June 30, 2021.

Private Placements of Common Stock, Non-Voting Preferred Stock and Warrants

On May 3, 2019, we entered into a securities purchase agreement (the "May 2019 SPA") with certain institutional and other accredited investors, including certain directors, executive officers and employees of the Company (the "Purchasers"), pursuant to which we agreed to sell and issue shares of our common stock, shares of our newly designated non-voting convertible preferred stock, and warrants to purchase common stock, in up to two closings, in a private placement transaction (the "Private Placement").

At an initial closing under the May 2019 SPA that occurred on May 7, 2019 (the "Initial Closing"), we sold and issued to the Purchasers (i) 9,730,534 shares of common stock and accompanying warrants to purchase up to an aggregate of 9,730,534 shares of common stock at a combined purchase price of \$1.205 per share, and (ii) 415,898 shares of non-voting Class A-1 convertible preferred stock, in lieu of shares of common stock, at a price of \$10.80 per share, and accompanying warrants to purchase an aggregate of 4,158,980 shares of common stock at a price of \$0.125 for each share of common stock underlying such warrants. Total gross proceeds from the Initial Closing were approximately \$16.7 million, which does not include any proceeds that may be received upon exercise of the warrants. Each share of non-voting Class A-1 convertible preferred stock is convertible into 10 shares of Common Stock, subject to certain beneficial ownership conversion limitations. The warrants are exercisable for a period of five years following the date of issuance and have an exercise price of \$1.08 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events. The warrants are exercisable on a net exercise "cashless" basis. An aggregate of 526,083 shares of common stock and warrants to purchase up to 526,083 shares of common stock were purchased for \$0.6 million by certain directors and executive officers of the Company under the Initial Closing.

Pursuant to the May 2019 SPA, in the event our Board of Directors unanimously resolved to recommence our Phase 1 multiple ascending dose clinical trial of our RGLS4326 product candidate for the treatment of ADPKD (the "Phase 1 Trial") based on correspondence from the U.S. Food and Drug Administration's Division of Cardiovascular and Renal Products, and thereafter but on or before December 31, 2019, we made a public announcement of our plan to recommence the Phase 1 Trial (the "Public Announcement"), we would sell and the Purchasers would purchase, at a second closing under the May 2019 SPA ("Milestone Closing"), shares of our non-voting convertible preferred stock and accompanying warrants to purchase shares of Common Stock (collectively, "Milestone Securities"). On December 15, 2019, the Company's Board of Directors unanimously resolved to recommence the Phase 1 Trial based on correspondence from the U.S. Food & Drug Administration's Division of Cardiovascular and Renal Products and on December 16, 2019, we made the related Public Announcement, triggering the Milestone Closing, which occurred on December 24, 2019. At the Milestone Closing, we sold and issued to the Purchasers 3,288,390 shares of non-voting Class A-2 convertible preferred stock and accompanying warrants to purchase an aggregate of 32,883,900 shares of common stock for an aggregate purchase price of approximately \$26.0 million. Net proceeds to the Company from the Milestone Closing were approximately \$24.6 million. Each share of non-voting Class A-2 convertible preferred stock is convertible into 10 shares of Common Stock, subject to certain beneficial ownership conversion limitations. The warrants will be exercisable for a period of five years following the date of issuance and have an exercise price of \$0.666 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events. The warrants are exercisable on a net exercise "cashless" basis. An aggregate of 121,581 shares of Class A-2 convertible preferred stock and warrants to purchase up to 1,215,810 shares of common stock were purchased for approximately \$1.0 million by certain directors and executive officers of the Company under the Milestone Closing.

We evaluated the non-voting Class A-1 convertible preferred stock and common stock warrants sold in the Initial Closing and the Class A-2 convertible preferred stock and common stock warrants sold in the Milestone Closing under ASC 480, Distinguishing Liabilities from Equity, and ASC 815, Derivatives and Hedging, and determined permanent equity treatment was appropriate for these freestanding financial instruments. The Initial Closing and Milestone Closing did not include any embedded features that required bifurcation. The non-voting Class A-2 convertible preferred stock and warrants issuable under the Milestone Closing were not subject to accounting recognition until the Milestone Closing occurred, as the terms of the Milestone Closing did not provide a right or an obligation on either the Company nor the Purchasers.

On December 1, 2020, we entered into a Securities Purchase Agreement (the "December 2020 SPA") with certain institutional and other accredited investors, including certain directors, executive officers and employees of the Company (the "2020 Purchasers"), pursuant to which we agreed to sell and issue shares of our common stock, shares of newly designated non-voting convertible preferred stock and warrants to purchase common stock (the "2020 PIPE").

At the closing under the December 2020 SPA that occurred on December 4, 2020 (the "2020 Closing"), we sold and issued to the 2020 Purchasers (i) 24,341,607 shares of common stock and accompanying warrants to purchase up to an aggregate of 18,256,204 shares of common stock at a combined purchase price of \$0.7464 per share, and (ii) 272,970 shares of non-voting Class A-3 convertible preferred stock, in lieu of shares of common stock, at a price of \$6.22 per share, and accompanying warrants to purchase an aggregate of 2,047,276 shares of common stock at a price of \$0.125 for each share of common stock underlying such warrants. Total gross proceeds from the 2020 Closing were approximately \$19.4 million, which does not include any proceeds that may be received upon exercise of the warrants. Each share of non-voting Class A-3 convertible preferred stock is convertible into 10 shares of common stock, subject to certain beneficial ownership conversion limitations. The warrants are exercisable for a period of five years following the date of issuance and have an exercise price of \$0.622 per share, subject to proportional adjustments in the event of stock splits or combinations or similar events. The warrants are exercisable on a net exercise "cashless" basis. An aggregate of 833,208 shares of common stock and warrants to purchase up to 624,906 shares of common stock were purchased for \$0.6 million by certain directors and executive officers of the Company at the 2020 Closing.

We evaluated the non-voting Class A-3 convertible preferred stock and common stock warrants sold in the 2020 PIPE under ASC 480, Distinguishing Liabilities from Equity, and ASC 815, Derivatives and Hedging, and determined permanent equity treatment was appropriate for these freestanding financial instruments and there were no embedded features that required bifurcation.

The following table summarizes preferred stock conversions and warrant exercises (and the related impact on common stock) under the 2019 SPA and 2020 SPA for the three and six months ended June 30, 2021 and 2020 (in thousands):

	Class A-1 Convertible Preferred Stock	Class A-2 Convertible Preferred Stock	Class A-3 Convertible Preferred Stock	Warrants	Com Stock
Balance at December 31, 2020	257	1,416	259	66,038	
Conversions/Exercises	—	(78)	—	(3,920)	3,
Balance at March 31, 2021	257	1,338	259	62,118	
Conversions/Exercises	—	(7)	—	(250)	
Balance at June 30, 2021	257	1,331	259	61,868	
Balance at December 31, 2019	416	3,288	—	46,774	
Conversions/Exercises	—	(656)	—	—	6,
Balance at March 31, 2020	416	2,632	—	46,774	
Conversions/Exercises	(159)	(671)	—	—	8,
Balance at June 30, 2020	257	1,961	—	46,774	

ATM Offering

On December 12, 2018, we entered into a Common Stock Sales Agreement (the "Stock Sales Agreement") with H.C. Wainwright & Co., LLC ("HCW"), pursuant to which we may sell and issue shares of our common stock from time to time through HCW, as our sales agent (the "ATM Offering"). We have no obligation to sell any shares of common stock in the ATM Offering, and may at any time suspend offers under the Stock Sales Agreement or terminate the Stock Sales Agreement.

Subject to the terms and conditions of the Stock Sales Agreement, HCW will use its commercially reasonable efforts to sell shares of our common stock from time to time based upon our instructions (including any price, time or size limits or other parameters or conditions the we may impose, subject to certain restrictions). We pay HCW a commission of 3.0% of the gross sales price of any shares sold under the Stock Sales Agreement. A total of 12,007,546 shares were sold and settled for proceeds of \$14.8 million (net of \$0.5 million in commissions) under the ATM Offering during the three months ended June 30, 2021. A total of 16,017,131 shares were sold and settled for proceeds of \$20.5 million (net of \$0.8 million in offering costs) under the ATM Offering during the six months ended June 30, 2021. No shares were sold under the ATM Offering during the three and six months ended June 30, 2020. At June 30, 2021, approximately \$13.6 million remained available for sale in the ATM Offering. On August 10, 2021, we increased the amount of common stock available for sale in ATM Offerings under the Stock Sales Agreement to \$50.0 million

Shares Reserved for Future Issuance

The following shares of common stock were reserved for future issuance as of June 30, 2021 (in thousands):

Class A-1 convertible preferred stock outstanding (as-converted)	2,567
Class A-2 convertible preferred stock outstanding (as-converted)	13,308
Class A-3 convertible preferred stock outstanding (as-converted)	2,587
2019 PIPE Initial Closing warrants	12,778
2019 PIPE Milestone Closing warrants	30,595
2020 PIPE warrants	18,495
Common stock options outstanding	9,557
RSUs outstanding	446
Common stock available for future grant under 2019 Equity Incentive Plan	1,023
Employee Stock Purchase Plan	267
Total common shares reserved for future issuance	91,623

The following table summarizes our stock option and RSU (together Stock Awards) activity under all equity incentive plans for the six months ended June 30, 2021 (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, 2020	6,813	\$ 1.10	34	\$ 1.50
Granted	2,973	\$ 1.51	446	\$ 0.95
Exercised (options) or Vested (RSUs)	(28)	\$ 0.96	(34)	\$ 1.50
Canceled/forfeited/expired	(201)	\$ 1.22	—	\$ 1.50
Stock Awards outstanding at June 30, 2021	9,557	\$ 1.23	446	\$ 0.95

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, 2015 Inducement Plan, 2019 Equity Incentive Plan and the shares purchasable under our Employee Stock Purchase Plan during the periods presented:

	Three months ended June 30,		Six months ended June 30,	
	2021	2020	2021	2020
Stock options				
Risk-free interest rate	1.1 %	3.9 %	1.0 %	1.3 %
Volatility	96.5 %	95.4 %	95.8 %	95.4 %
Dividend yield	—	—	—	—
Expected term (years)	6.1	6.1	6.1	6.1
Performance stock options				
Risk-free interest rate	—	—	1.0 %	1.4 %
Volatility	—	—	95.7 %	95.4 %
Dividend yield	—	—	—	—
Expected term (years)	0	0	6.1	6.1
Employee stock purchase plan shares				
Risk-free interest rate	0.1 %	0.4 %	0.1 %	0.9 %
Volatility	108.9 %	93.7 %	105.1 %	99.8 %
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 June 30,		Six months ended June 30,	
	2021	2020	2021	2020
Research and development	\$ 229	\$ 159	\$ 410	\$ 316
General and administrative	525	470	1,035	1,136
Total	\$ 754	\$ 629	\$ 1,445	\$ 1,452

7. Collaborations

Revenue recognized from our strategic collaborations was zero for the three and six months ended June 30, 2021, and zero and less than \$0.1 million for the three and six months ended June 30, 2020, respectively.

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. The following elements were delivered as part of the strategic collaboration with Sanofi: (1) a license for up to four *microRNA* targets; and (2) a research license under our technology collaboration.

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 February 2014, we and Sanofi entered into a second amended and restated collaboration and license agreement (the “2014 Sanofi Amendment”) to discover, develop and commercialize *microRNA* therapeutics to focus on specific orphan disease and oncology targets. Under the terms of the 2014 Sanofi Amendment, Sanofi had 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 were responsible for developing each of these programs to proof-of-concept, at which time Sanofi had an exclusive option on each program. If Sanofi chooses to exercise its option on any of these programs, Sanofi would reimburse us for a significant portion of our preclinical and clinical development costs and would 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 relating to our preclinical program targeting miR-221/222. As indicated below, we entered into an additional amendment with Sanofi in November 2018, under which Sanofi's opt-in rights to our miR-21 programs under the 2014 Sanofi Amendment were relinquished. Sanofi's opt-in rights with regard to our miR-221/222 preclinical program under the 2014 Sanofi Amendment remained unchanged.

We are eligible to receive milestone payments related to the development and commercialization of miR-221/222 for HCC of up to \$38.8 million for proof-of-concept option exercise fees (net of \$1.25 million creditable, as noted above), \$25.0 million for clinical milestones and up to \$130.0 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-221/222 program 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 miR-221/222 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.

In November 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, product-specific patents 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 were eligible to receive approximately \$6.8 million in upfront payments for the license and for miR-21 program-related materials (collectively, the "Upfront Amendment Payments"). We were also eligible to receive up to \$40.0 million in development milestone payments, including a \$10.0 million payment for an interim enrollment milestone (the "Enrollment Milestone"). In addition, Sanofi has agreed to reimburse us for certain out-of-pocket transition activities and assume our upstream license royalty obligations. In 2019, we completed the performance obligations under the 2018 Sanofi Amendment and recognized revenue for the \$6.8 million in Upfront Amendment Payments.

In August 2020, we entered into an amendment to the 2018 Sanofi Amendment (the "2020 Sanofi Amendment"). Under the terms of the 2020 Sanofi Amendment, we agreed to transfer to Sanofi additional RG-012 development program materials (the "Materials") in exchange for a payment from Sanofi of \$1.0 million (the "Transfer Payment"). In addition, in lieu of the \$10.0 million Enrollment Milestone under the 2018 Sanofi Amendment, Sanofi agreed to pay us a \$4.0 million milestone upon the completion of the transfer and verification of the Materials, and \$5.0 million upon achievement of the Enrollment Milestone. Additionally, we are eligible to receive \$25.0 million upon achievement of an additional development milestone related to Sanofi's development of the miR-21 compounds. In September 2020, we received \$1.0 million in exchange for the transfer of the Materials to Sanofi, and received an additional \$4.0 million in October 2020 as a result of Sanofi's completion and verification of the Materials in September 2020. As the performance obligations associated with both of these payments had been satisfied under Topic 606 as of September 30, 2020, both amounts were recognized as revenue in the third quarter of 2020. In November 2020, we received \$5.0 million upon achievement of the Enrollment Milestone. As the performance obligations associated with this payment had been satisfied under Topic 606 as of December 31, 2020, this amount was recognized as revenue in the fourth quarter of 2020.

As of June 30, 2021, the \$25.0 million in development milestone payments (variable consideration) is fully constrained and therefore, does not meet the criteria for revenue recognition.

8. Leases

At the inception of a contractual arrangement, we determine whether the contract contains a lease by assessing whether there is an identified asset and whether the contract conveys the right to control the use of the identified asset in exchange for consideration over a period of time. For operating leases with an initial term greater than 12 months, we recognize operating lease right of use assets ("ROU assets") and operating lease liabilities based on the present value of lease payments over the lease term at the commencement date. Operating lease ROU assets are comprised of the lease liability plus any lease payments made and excludes lease incentives. Lease terms include options to renew or terminate the lease when we are reasonably certain that the renewal option will be exercised or when it is reasonably certain that the termination option will not be exercised. For

our operating leases, we generally cannot determine the interest rate implicit in the lease, in which case we use our incremental borrowing rate as the discount rate for the lease. We estimate our incremental borrowing rate for our operating leases based on what we would normally pay to borrow on a collateralized basis over a similar term for an amount equal to the lease payments. Operating lease expense is recognized on a straight-line basis over the lease term. Leases with a lease term of 12 months or less are not recorded on the unaudited condensed balance sheet. Instead, we recognize lease expense for these leases on a straight-line basis over the lease term. Our lease agreements do not contain any material variable lease payments, residual value guarantees or restrictive covenants. Certain leases require us to pay taxes, insurance, utilities, and maintenance costs for the building, which do not represent lease components. We elected to not separate lease and non-lease components.

On June 19, 2019, we entered into a lease agreement (the "Prior Lease") with ARE SD Region No.44 LLC ("Landlord") for the lease of approximately 8,727 square feet of rentable area of the building located at 10628 Science Center Drive, Suite 225, San Diego, California 92121 (the "Prior Premises"). The commencement date of the Prior Lease was July 1, 2019 (the "Prior Commencement Date"). We used the Prior Premises as our principal executive offices and as a laboratory for research and development and other related uses. The term of the Prior Lease (the "Prior Initial Term") was two years, six months, ending December 31, 2021. The base rent payments due for the Prior Premises were \$0.4 million in 2020 and \$0.4 million in 2021, net of certain rent abatement terms. We were also responsible for the payment of additional rent to cover our share of the annual operating expenses of the building, the annual tax expenses of the building and the annual utilities cost of the building.

On July 1, 2019, we recorded a \$0.8 million lease liability for the Prior Lease, which was calculated as the present value of future lease payments to be made under the Prior Lease. A \$0.6 million ROU asset was also recorded on July 1, 2019, which represents the difference between the lease liability and the remaining \$0.2 million deferred credit for the reduction of the lease liability under the operating lease agreement with Landlord dated February 25, 2019.

On February 11, 2021, we entered into a lease agreement (the "Campus Point Lease") with ARE-SD Region No. 61, LLC (as successor in interest to ARE-SD Region No. 58, LLC) ("Campus Point Landlord"), for the lease of approximately 13,438 square feet of rentable area located at 4224 Campus Point Court, Suite 210, San Diego, California, 92121 (the "Campus Point Premises"). The commencement date of the Campus Point Lease was April 15, 2021. However, for accounting purposes the lease commencement date was February 11, 2021. We are using the Campus Point Premises as our new principal executive offices and as a laboratory for research and development, manufacturing and other related uses. The term of the Campus Point Lease ("Campus Point Initial Term") is 60 months, ending April 30, 2026. The aggregate base rent due over the initial term of the Campus Point Lease is approximately \$3.8 million. We are also responsible for the payment of additional amounts to cover our share of the annual operating expenses of the building, the annual tax expenses of the building and the utilities costs for the building.

On February 11, 2021, concurrently with entry into the Campus Point Lease, we entered into an Assignment and Assumption of Lease (the "Assignment Agreement") with Turning Point Therapeutics, Inc. ("Assignee") and a Consent to Assignment (the "Consent") with Landlord. Pursuant to the Assignment Agreement, we will assign all rights, title, and interest under the New Lease to Assignee and delivered the New Premises to Assignee on April 22, 2021. Pursuant to the Assignment Agreement, Assignee paid us \$60,000 in non-refundable assignment consideration. Additionally, the Consent stipulates that we were not required to pay a fee pursuant to the Prior Lease in connection with the assignment.

The execution of the Campus Point Lease, Consent, and Assignment Agreement resulted in a modification which was not accounted for as a separate contract. Rather, we accounted for the three contracts with Campus Point Landlord in combination, as they were entered into at the same time and negotiated as a package to achieve the same commercial objective. We accounted for a \$0.2 million reduction in the lease liability for the Prior Lease as a deferred credit that is amortized as a reduction to rent expense over the term of the Campus Point Lease. A lease liability of less than \$0.1 million and ROU asset of less than \$0.1 million remained with respect to the Prior Lease and was fully amortized as of April 30, 2021. On February 11, 2021, we recorded a \$3.2 million lease liability for the Campus Point Lease, which was calculated as the present value of future lease payments to be made under the Campus Point Lease. A \$3.0 million ROU asset was also recorded on February 11, 2021, which represents the difference between the lease liability and the \$0.2 million deferred credit for the reduction of the lease liability under the Prior Lease.

Our future lease payments under operating leases at June 30, 2021 are as follows (in thousands):

	Operating Leases
Remaining 2021	\$ 341
2022	754
2023	776
2024	800
Thereafter	1,101
Total lease payments	\$ 3,772
Less: amount representing interest	(519)
Present value of obligations under leases	3,253
Less: current portion	(533)
Long-term lease obligations	\$ 2,720

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, 2020 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, 2020, or Annual Report, filed with the Securities and Exchange Commission on March 9, 2021. 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 the federal securities laws made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Our actual results could differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth below under Part II, Item 1A, "Risk Factors" in this quarterly report on Form 10-Q. Except as required by law, we assume no obligation to update these forward-looking statements, whether as a result of new information, future events or otherwise. These statements, which represent our current expectations or beliefs concerning various future events, may contain words such as "may," "will," "expect," "anticipate," "intend," "plan," "believe," "estimate" or other words indicating future results, though not all forward-looking statements necessarily contain these identifying words. Such statements may include, but are not limited to, statements concerning the following:

- the initiation, cost, timing, progress and results of, and our expected ability to undertake certain activities and accomplish certain goals with respect to our research and development activities, preclinical studies and clinical trials;
- our ability to obtain and maintain regulatory approval of our product candidates, and any related restrictions, limitations, and/or warnings in the label of an approved product candidate;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our product candidates;
- the potential election of any strategic 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 collaboration 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;
- the potential impact of the COVID-19 pandemic on our business; 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. ("Alnylam") and Ionis Pharmaceuticals, Inc. ("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. As a result, Sanofi became responsible for all costs incurred in the development of RG-012 and any other miR-21 programs. The transition activities were completed in the second quarter of 2019. RGLS4326, an anti-miR targeting miR-17, is in Phase 1 development for the treatment of autosomal dominant polycystic kidney disease ("ADPKD"). In addition to these clinical programs, we continue to develop a pipeline of preclinical drug product candidates.

microRNAs are naturally occurring ribonucleic acid ("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 ("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 ("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.

Since our inception through June 30, 2021, we have received \$384.0 million from the sale of our equity and convertible debt securities, \$101.8 million from our strategic collaborations, principally from upfront payments, research funding and preclinical and clinical milestones, and \$19.8 million in net proceeds from our Term Loan. As of June 30, 2021, we had cash and cash equivalents of \$41.4 million.

Development Stage Pipeline

We currently have two programs in clinical development.

RG-012: In May 2017, we completed a Phase 1 multiple-ascending dose ("MAD") clinical trial in 24 healthy volunteers (six-week repeat dosing) to determine safety, tolerability and pharmacokinetics ("PK") of RG-012 prior to chronic dosing in patients. In Phase 1 clinical trials to date, RG-012 was well-tolerated, and there were no serious adverse events ("SAEs") reported. In the third quarter of 2017, we initiated HERA, a Phase 2 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 PK, target engagement and downstream effects on genomic disease biomarkers. Kidney tissue concentrations were achieved in biopsy patients that would be predictive of therapeutic benefit based on animal disease models. In addition, modulation of the target, miR-21, was observed. In December 2017, we concluded our global ATHENA natural history of disease study. RG-012 has received orphan designation in both the United States and Europe. In November 2018, we and Sanofi agreed to transition further development activities of our miR-21 programs, including our RG-012 program to Sanofi. As a result, Sanofi became responsible for all costs incurred in the development of these miR-21 programs. The transition activities, including the transfer of the investigational new drug application ("IND"), were completed in the second quarter of 2019. Sanofi is currently enrolling patients into a Phase 2 clinical trial, with sites in the United States, Europe, Australia and China.

ADPKD Program

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 1 single ascending dose ("SAD") clinical trial in healthy volunteers and found RGLS4326 was well tolerated and no SAEs were reported. In April 2018, we initiated a Phase 1 randomized, double-blind, placebo-controlled, MAD clinical trial in healthy volunteers designed to characterize the safety, tolerability, PK 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 2 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 1 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.

In January 2019, we submitted a comprehensive data package for RGLS4326 to the U.S. Food and Drug Administration ("FDA") that included the results from the planned 13-week interim analysis of the ongoing repeat mouse chronic toxicity study, as well as results from additional investigations, analytical testing, additional data from the previously terminated mouse chronic toxicity study, data from the completed Phase 1 SAD study and data from the first cohort of the Phase 1 MAD study to support our plan to resume the Phase 1 MAD study. In July 2019, FDA notified us of additional nonclinical data requirements and placed the IND on a partial clinical hold, formalizing the specific requirements to re-initiate the MAD study and further proceed into studies of extended duration (the "FDA Partial Clinical Hold Letter"). The additional data requirements were outlined in two parts. In order to resume the MAD study, FDA requested the final reports from the chronic toxicity studies in both mice and non-human primates and satisfactory related analyses to ensure subjects can be safely dosed. In November 2019, we submitted a complete response to the partial clinical hold in order to be able to resume the MAD study and in December 2019, FDA lifted the partial clinical hold on the MAD study. In February 2020, we recommenced the MAD study and in August 2020 completed treatment and follow-up. RGLS4326 was well-tolerated with no serious adverse events reported. Results show that plasma exposure is dose proportional. In July 2020, the FDA granted orphan drug designation to RGLS4326 for the treatment of ADPKD.

In February 2021, we completed enrollment in the first cohort of a Phase 1b clinical study for RGLS4326 in patients with ADPKD. The Phase 1b clinical study is an adaptive design, open-label, multiple dose study in up to three cohorts of patients with ADPKD. The study is designed to evaluate the safety, pharmacokinetics, and changes in levels of polycystin 1 ("PC1") and polycystin 2 ("PC2") in patients with ADPKD administered RGLS4326 every other week for a total of four doses. The dose level for the first cohort is 1 mg/kg of RGLS4326 and the dose level for the second cohort is 0.3 mg/kg.

In May 2021, we announced top-line results from the first cohort of patients with ADPKD in our ongoing Phase 1b clinical trial of RGLS4326. In the first cohort, nine patients were enrolled and received 1 mg/kg of RGLS4326 subcutaneously every other week for four doses. The mean increase in polycystins 1 and 2 at the end of study compared to baseline levels for all nine patients in the first cohort were 58% (p=.0004) and 38% (p=.026) respectively. Treatment with RGLS4326 was generally well-tolerated with no serious adverse events reported. All reported adverse events were mild and generally transient in nature. We believe these data demonstrate that RGLS4326 engages the target miR-17 leading to increased expression of the PKD1 and PKD2 genes and the resultant increases in polycystins' levels. Levels of polycystin 1 (PC1) and polycystin 2 (PC2) have previously been shown to inversely correlate with disease severity and are believed to be directly linked to the underlying genetic drivers of the disease.

In June 2021, we presented additional data from the first cohort of patients in our Phase 1b clinical trial of RGLS4326 for the treatment of ADPKD, as well as new preclinical data from relevant animal models of the disease, at PKD Connect 2021. The additional data presented at PKD Connect demonstrated clinical proof of mechanism by showing statistically significant increases in polycystin levels in ADPKD patients by targeting miR-17 in the kidneys.

The Company also presented new data from relevant preclinical models showing treatment with RGLS4326 resulted in increased gene and polycystin levels in vitro. Improvements in key disease markers including serum creatinine and BUN were demonstrated in the Pkd1(F/RC) mouse model that harbors a mutation in the Pkd1 gene equivalent to human ADPKD. Mutation to the Pkd1 gene is reported for 85% of diagnosed patients with ADPKD.

In late July 2021, we completed enrollment of the second cohort of patients in the Phase 1b clinical study of RGLS4326. The dose of RGLS4326 for the third and final cohort will be chosen based on the results of this second cohort and enrollment is expected to commence in the fourth quarter of 2021. We expect to report top-line data from the second cohort in the fourth quarter of 2021.

We requested a Type A meeting with FDA to discuss the data supporting our approach to addressing the remaining FDA partial clinical hold requirements. FDA typically responds to a sponsor's request with the meeting being scheduled within 30 days from the receipt of the meeting request.

RGLS8429: We nominated RGLS8429 as a clinical candidate with an Investigational New Drug ("IND") submission planned for Q1 2022. RGLS8429 has been designed as a next-generation compound for the treatment of ADPKD by inhibiting the role of miR-17 in the kidney. RGLS8429 has completed an extensive 14-week toxicity study in mice at significantly higher doses than RGLS4326 and has shown an overall enhanced profile.

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, oncology 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 have multiple programs in various stages of preclinical development. While

we are not currently advancing these programs to IND, we are working to explore the potential of microRNAs in these therapeutic areas.

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 250 million people worldwide. Our lead compound directed to one of the host microRNAs has demonstrated reduction of both HBV DNA replication surface antigen in both in vitro and in vivo 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 are currently optimizing our development candidate for HBV.

Cell Therapy program: Cell therapies have been approved to treat a variety of hematological malignancies. Targeting solid tumors, however, has proven challenging for cell therapies due to various factors including the immune-suppressive effect of the tumor microenvironment ("TME"). We have demonstrated that ex vivo modulation of microRNA can improve many characteristics of engineered cells and may enable cell therapy approaches to overcome challenges posed by the TME. We are pursuing applications of microRNA technology in cell therapies. We are seeking a partner to collaborate on this program.

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 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 collaborations. 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 collaboration partners. If our current or future collaboration partners do not elect or otherwise agree to fund our development costs pursuant to our current or future strategic collaboration agreements, or we or our strategic collaboration 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, amortization 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 most promising 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 incurred a total of approximately \$380.9 million in research and development expenses through June 30, 2021.

The process of conducting clinical trials and preclinical studies necessary to obtain regulatory approval is costly and time consuming. We, or our strategic collaboration 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 collaborations 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 collaborations 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 marketable securities, such as interest-bearing bonds, for our short-term investments. Interest expense is primarily attributable to interest charges associated with borrowings under our secured Term Loan.

CRITICAL ACCOUNTING POLICIES AND ESTIMATES

There have been no significant changes to our critical accounting policies since December 31, 2020. For a description of critical accounting policies that affect our significant judgments and estimates used in the preparation of our financial statements, refer to Item 7 in Management's Discussion and Analysis of Financial Condition and Results of Operations and Note 1 to our financial statements contained in our Annual Report and Note 1 to our condensed financial statements contained in this quarterly report on Form 10-Q.

RESULTS OF OPERATIONS

Comparison of the three and six months ended June 30, 2021 and 2020

The following table summarizes our results of operations for the three and six months ended June 30, 2021 and 2020 (in thousands):

	Three months ended June 30,		Six months ended June 30,	
	2021	2020	2021	2020
Revenue under collaborations	\$ —	\$ —	\$ —	\$ 6
Research and development expenses	4,150	4,242	7,470	7,360
General and administrative expenses	2,488	2,254	4,967	4,676
Interest and other income (expenses), net	605	(451)	391	(862)

Revenue under collaborations

Our revenues are generated from ongoing 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 was zero for

each the three and six months ended June 30, 2021, compared to zero and less than \$0.1 million for the three and six months ended June 30, 2020, respectively.

Research and development expenses

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

	Three months ended June 30, 2021		Three months ended June 30, 2020		Increase (decrease)	
	\$	% of total	\$	% of total	\$	%
Research and development						
Personnel and internal expenses	\$ 1,534	37 %	\$ 1,354	32 %	\$ 180	13 %
Third-party and outsourced expenses	2,346	56 %	2,611	61 %	(265)	(10)%
Non-cash stock-based compensation	229	6 %	159	4 %	70	44 %
Depreciation	41	1 %	118	3 %	(77)	(65)%
Total research and development expenses	\$ 4,150	100 %	\$ 4,242	100 %	\$ (92)	(2)%

	Six months ended June 30, 2021		Six months ended June 30, 2020		Increase (decrease)	
	\$	% of total	\$	% of total	\$	%
Research and development						
Personnel and internal expenses	\$ 3,055	41 %	\$ 2,648	36 %	\$ 407	15 %
Third-party and outsourced expenses	3,633	49 %	4,159	57 %	(526)	(13)%
Non-cash stock-based compensation	410	5 %	316	4 %	94	30 %
Depreciation	372	5 %	237	3 %	135	57 %
Total research and development expenses	\$ 7,470	100 %	\$ 7,360	100 %	\$ 110	1 %

Research and development expenses were \$4.2 million and \$7.5 million for the three and six months ended June 30, 2021, compared to \$4.2 million and \$7.4 million for the three and six months ended June 30, 2020. These amounts reflect the internal and external costs associated with advancing our clinical and preclinical pipeline.

General and administrative expenses

General and administrative expenses were \$2.5 million and \$5.0 million for the three and six months ended June 30, 2021, compared to \$2.3 million and \$4.7 million for the three and six months ended June 30, 2020. These amounts reflect personnel-related and ongoing general business operating costs.

Interest and other income (expenses), net

Net interest and other income was \$0.6 million and \$0.4 million for the three and six months ended June 30, 2021, respectively, which included a \$0.7 million gain on forgiveness of our PPP loan during the three months ended June 30, 2021, partially offset by interest charges associated with our outstanding Term Loan. Net interest and other expenses were \$0.5 million and \$0.9 million for the three and six months ended June 30, 2020, respectively. These amounts were primarily related to interest charges associated with our outstanding Term Loan.

LIQUIDITY AND CAPITAL RESOURCES

Since our inception through June 30, 2021, we have received \$384.0 million from the sale of our equity and convertible debt securities, \$101.8 million from our collaborations, principally from upfront payments, research funding and preclinical and clinical milestones, and \$19.8 million in net proceeds from our Term Loan. As of June 30, 2021, we had cash and cash equivalents of \$41.4 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 our 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 collaboration and license agreement with Sanofi;
- the terms and timing of any other strategic collaboration, 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, and the pricing and reimbursement for any products for which we may receive regulatory approval;
- 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 six months ended June 30, 2021 and 2020 (in thousands):

	Six months ended June 30,	
	2021	2020
	(unaudited)	
Net cash (used in) provided by:		
Operating activities	\$ (10,735)	\$ (11,228)
Investing activities	(184)	—
Financing activities	21,334	526
Total	\$ 10,415	\$ (10,702)

Operating activities

Net cash used in operating activities was \$10.7 million for the six months ended June 30, 2021, compared to \$11.2 million for the six months ended June 30, 2020. The decrease in net cash used in operating activities was primarily attributable to a decrease in net loss of \$0.8 million for the six months ended June 30, 2021, compared to the same period in 2020, partially offset by a \$0.3 million change in working capital for the six months ended June 30, 2021, compared to the same period in 2020.

Investing activities

Net cash used in investing activities was \$0.2 million for the six months ended June 30, 2021, compared to zero for the six months ended June 30, 2020. Net cash used in investing activities for the six months ended June 30, 2021 was attributable to lab equipment purchases.

Financing activities

Net cash provided by financing activities was \$21.3 million for the six months ended June 30, 2021, compared to net cash provided by financing activities of \$0.5 million for the six months ended June 30, 2020. Net cash provided by financing

activities for the six months ended June 30, 2021 was primarily attributable to proceeds from the issuance of our common stock under our ATM Offering.

CONTRACTUAL OBLIGATIONS AND COMMITMENTS

As of June 30, 2021, there have been no material changes, outside of the ordinary course of business, in our outstanding contractual obligations from those disclosed in Note 8 Commitments and Contingencies, Note 9 Debt, and Note 13 Leases to our financial statements contained in our Annual Report, with the exception of the Campus Point Lease, Assignment Agreement and Consent with Campus Point Landlord concerning our new corporate headquarters and the assignment of our previous corporate headquarters (refer to Note 8 to our condensed financial statements contained in this quarterly report on Form 10-Q), and full forgiveness of our \$0.7 million PPP Loan (refer to Note 5 to our condensed financial statements contained in this quarterly report on Form 10-Q).

OFF-BALANCE SHEET ARRANGEMENTS

As of June 30, 2021, 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 and cash equivalents. We invest our excess cash primarily in money market funds. 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 investments without significantly increasing risk. We have 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, we do not believe that an increase in market rates would have any significant impact on the realized value of our cash equivalents. If a 10% change in interest rates were to have occurred on June 30, 2021, this change would not have had a material effect on the fair value of our cash equivalents as of that date.

We also have interest rate exposure as a result of our outstanding Term Loan. As of June 30, 2021, the outstanding principal amount of the Term Loan was \$4.7 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. LIBOR is currently scheduled to be phased out by the end of 2021. Before LIBOR is phased out, we may need to renegotiate the Term Loan to replace LIBOR with the Secured Overnight Financing Rate ("SOFR"). The consequences of these developments cannot be entirely predicted, but could result in higher interest rates on the principal amount of the Term Loan.

If a 10% change in interest rates were to have occurred on June 30, 2021, 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 officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based, in part, upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, controls may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

As of June 30, 2021, we carried out an evaluation, under the supervision and with the participation of our management, including our principal executive officer and our principal financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended. Based on this evaluation, our principal executive officer and our principal financial officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of June 30, 2021.

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 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

We currently are not a party to any legal proceedings, the adverse outcome of which, in management's opinion, individually or in the aggregate, would have a material adverse effect on our results of operations or financial position.

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 () 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 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 collaboration 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 collaboration partners may change their development profiles for potential product candidates or abandon a therapeutic area.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

Preclinical 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 collaboration 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 July 2018, we voluntarily paused our Phase 1 MAD clinical trial for RGLS4326 due to unexpected observations in our 27-week mouse chronic toxicity study, which was designed to support the Phase 2 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 1 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. In January 2019, we announced data from a planned interim analysis of this study after 13 weeks of dosing in which no adverse or other significant findings across the range of doses tested were shown. We submitted a comprehensive data package for RGLS4326 to FDA that included the results from the planned 13-week interim analysis of the ongoing repeat mouse chronic toxicity study, as well as results from additional investigations, analytical testing, additional data from the previously terminated mouse chronic toxicity study, data from the completed Phase 1 SAD study and data from the first cohort of the Phase 1 MAD study to support our plan to resume the Phase 1 MAD study. In July 2019, FDA notified us of additional nonclinical data requirements and placed the IND on a partial clinical hold, formalizing the specific requirements to initiate the MAD study and further proceed into chronic dosing. The additional data requirements have been outlined in two parts. In order to resume the MAD study, FDA requested the final reports from the chronic toxicity studies in both mice and non-human primates and satisfactory related analyses to ensure subjects can be safely dosed. In November 2019, we submitted a complete response to the partial clinical hold in order to be able to resume the MAD study and in December 2019 FDA lifted the partial clinical hold of the MAD study. We recommenced the MAD study in February 2020 and have completed all dosing. Information from the clinical studies, together with information from additional nonclinical studies, will be used to address the requirements to support studies of extended duration. In addition to the MAD study in healthy volunteers, we have initiated a Phase 1b study in patients with ADPKD to evaluate RGLS4326 for safety, PK, and changes in levels of PC1 and PC2. We cannot be certain that we will be able to satisfy the requirements to initiate studies of extended duration in a timely manner, or at all.

In addition, enrollment and retention of patients in clinical trials could be disrupted by man-made or natural disasters, public health pandemics or epidemics or other business interruptions, including the ongoing COVID-19 pandemic. For example, we expect new site initiation and patient enrollment has been delayed in the RG-012 Phase 2 clinical trial being conducted by Sanofi. In addition, COVID-19 has, and may continue to, impact site initiation activities and subsequent study enrollment for our RGLS4326 clinical trials.

If we or our current or future collaboration 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 collaboration 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 collaboration 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 ("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 collaboration partner may develop under an agreement with us, our or our collaboration partners' ability to obtain regulatory approval for product candidates may be negatively impacted.

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

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

Any of these events could prevent us or our collaboration 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 collaboration 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 collaboration 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 collaboration 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 ("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.

Moreover, the FDA closely regulates the marketing, labeling, advertising and promotion of pharmaceutical products. A company can make only those claims relating to safety and efficacy, purity and potency that are approved by the FDA and in accordance with the provisions of the approved label. Companies may also share truthful and not misleading information that is otherwise consistent with the labeling. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses. Failure to comply with these requirements can result in significant civil, criminal and administrative penalties. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA made in the physician's independent medical judgement. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

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

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

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

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

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate

return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

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

Because we have limited financial and human resources, our existing strategy is to pursue collaboration agreements for the development and commercialization of our programs and potential product candidates in indications with potentially large commercial markets such as ADPKD, HCC, fibrosis 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 collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

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

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

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

RISKS RELATED TO OUR 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 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 June 30, 2021, we had approximately \$41.4 million of cash and cash equivalents and we had \$6.0 million of outstanding debt obligations (which includes \$4.7 million of outstanding principal and \$1.3 million of final payment and loan amendment fees) under our Term Loan. We will need to raise additional capital to fund our operations and service our debt obligations, 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.

Additionally, our collaboration partners may not elect to pursue the development and commercialization of any of our *microRNA* product candidates that are subject to their respective collaboration agreements with us. Any of these events may increase our development costs more than we expect. 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 collaborations 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 collaborations, or amend existing collaborations, 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.

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 Agreement with the Lender. Under the terms of the Loan Agreement, the Lender provided us with a \$20.0 million Term Loan. 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 assets that were licensed, assigned and transferred to Sanofi pursuant to the 2018 Sanofi Amendment that modify the parties' rights and obligations with respect to our miR-21 programs, including our RG-012 program, provided that the Lender will continue to have liens on all proceeds received by us pursuant to the Sanofi License Agreement. We have also agreed not to encumber our intellectual property assets, except as permitted by the Loan Agreement. Our required monthly payments to the Lender are comprised of interest only through and including the payment to be made in December 2021. We are required to maintain \$3.0 million in cash in a collateral account. During the first quarter of 2021, we received a waiver from the Lender with respect to noncompliance with a covenant under the Loan Agreement. We are in compliance with all Loan Agreement covenants as of the date of the filing of this Form 10-Q.

Amounts outstanding under the Term Loan mature on May 1, 2022.

Under the Term Loan, our interest rate on borrowed amounts is dependent on LIBOR. LIBOR is the basic rate of interest used in lending between banks on the London interbank market and is widely used as a reference for setting the interest rate on loans globally. In July 2017, the Chief Executive of the United Kingdom Financial Conduct Authority ("FCA"), which regulates LIBOR, announced that the FCA intends to phase out the use of LIBOR by the end of 2021. In addition, the U.S. Federal Reserve, in conjunction with the Alternative Reference Rates Committee, a steering committee comprised of large U.S. financial institutions, is considering replacing LIBOR with SOFR, a new index calculated by short-term repurchase agreements,

backed by Treasury securities. Although there have been certain issuances utilizing SOFR, it is unknown whether this or any other alternative reference rate will attain market acceptance as a replacement for LIBOR. The consequences of these developments cannot be entirely predicted, but could result in higher interest rates on our outstanding principal amount under the Term Loan. We cannot provide assurance that future interest rate changes will not have a material negative impact on our business, financial position, or operating results.

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.

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 loss was \$6.0 million and \$12.0 million for the three and six months ended June 30, 2021, compared to \$6.9 million and \$12.9 million for the three and six months ended June 30, 2020. As of June 30, 2021, we had an accumulated deficit of \$439.1 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 collaboration partners. We have a collaboration with Sanofi relating to the development of 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 collaboration for such product candidate. Pursuant to the 2018 Sanofi Amendment, we completed the transition of further development activities of our miR-21 programs, including our RG-012 program, to Sanofi, in the second quarter of 2019. As a result, Sanofi became responsible for all costs incurred in the development of our miR-21 programs.

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, collaborations or grants. We re-initiated clinical development of RGLS4326 for the treatment of ADPKD. We had also initiated clinical development of RG-012, which we subsequently transferred to Sanofi. Even if we or a collaboration partner successfully obtains 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 collaboration 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 collaboration 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 a collaboration 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.

RISKS RELATED TO OUR RELIANCE ON THIRD PARTIES

We will depend upon collaborations for the development and eventual commercialization of certain *microRNA* product candidates. If these collaborations 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 collaboration partners for financial and scientific resources for the clinical development and commercialization of certain of our *microRNA* product candidates. These collaborations 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 strategic collaboration 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 collaboration 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. As a result, Sanofi became responsible for all costs incurred in the development of our miR-21 program, but we will not receive royalties in the event our miR-21 programs are eventually commercialized, and the milestone payments we are eligible to receive for these programs has been significantly reduced.

Our ability to recognize revenues from successful collaborations may be impaired by several factors including:

- a collaboration 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;
- a collaboration partner may cease development in therapeutic areas which are the subject of our collaborations;
- a collaboration 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 a collaboration partner will also delay payment of milestones tied to such activities, thereby impacting our ability to fund our own activities;
- a collaboration partner could develop a product that competes, either directly or indirectly, with a collaboration product;
- a collaboration partner with commercialization obligations may not commit sufficient financial or human resources to the marketing, distribution or sale of a product;
- a collaboration partner with manufacturing responsibilities may encounter regulatory, resource or quality issues and be unable to meet demand requirements;
- a collaboration partner may exercise its rights under the agreement to terminate the collaboration;
- a dispute may arise between us and a collaboration 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
- a collaboration 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 collaboration or its current collaboration 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.

If Sanofi does not elect to pursue the development and commercialization of the *micro*RNA development candidates covered by our collaboration and license agreement with Sanofi or if Sanofi terminates the agreement, then, depending on the event:

- 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 by Sanofi;
- 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 Sanofi agreement, including the reimbursement of third parties; and
- in order to fund further development and commercialization, we may need to seek out and establish alternative collaborations 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 could 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 collaboration partners to select viable product candidates for IND submissions and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize such product candidates.

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

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

- the inability to meet any product specifications and quality requirements consistently;
- a delay or inability to procure or expand sufficient manufacturing capacity;
- manufacturing and product quality issues related to scale-up of manufacturing;
- costs and validation of new equipment and facilities required for scale-up;
- a failure to comply with cGMP and similar foreign standards;
- the inability to negotiate manufacturing or supply agreements with third parties under commercially reasonable terms;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us;
- the reliance on a limited number of sources, and in some cases, single sources for raw materials, such that if we are unable to secure a sufficient supply of these product components, we will be unable to manufacture and sell future product candidates in a timely fashion, in sufficient quantities or under acceptable terms;
- the lack of qualified backup suppliers for any raw materials that are currently purchased from a single source supplier;
- operations of our third-party manufacturers or suppliers could be disrupted by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier;
- carrier disruptions or increased costs that are beyond our control;
- disruptions caused by man-made or natural disasters or public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic; 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 collaboration 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 is 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, delay milestone payments owed to us or cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to deliver the required commercial quantities of active pharmaceutical ingredients on a timely basis and at commercially reasonable prices, and we are unable to secure one or more replacement suppliers capable of production in a timely manner at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

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

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

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

We or our collaboration 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 collaboration partners have limited influence over their actual performance. We control only certain aspects of our CROs' activities. Nevertheless, we or our collaboration 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 collaboration partners and our CROs are required to comply with the FDA's or other regulatory agency's good clinical practices ("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. 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 collaboration 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 collaboration 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.

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 collaboration 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, our exclusive license agreements with our founding companies, Alnylam and Ionis, provide us with rights to nucleotide technologies in the field of *micro*RNA therapeutics based on oligonucleotides that modulate *micro*RNAs. Some of these technologies, such as intellectual property relating to the chemical modification of oligonucleotides, are relevant to our product candidate development programs. If our license agreements with Alnylam or Ionis are terminated, or our business relationships with either of these companies or our other licensors are disrupted by events that may include the acquisition of either company, our access to critical intellectual property rights will be materially and adversely affected.

We may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

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

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

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

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

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

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

RISKS RELATED TO COMMERCIALIZATION OF PRODUCT CANDIDATES

The commercial success of our programs that are part of our collaboration agreements with Sanofi or others will depend in large part on the development and marketing efforts of our collaboration partners. If our collaboration 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. The transition activities were completed in the second quarter of 2019. As a result, we have no influence and/or control over their approaches to development and commercialization of our miR-21 programs. If Sanofi or any potential future collaboration 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 collaboration partners could be delayed or terminated. If we terminate any of our collaborations 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
- 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 and 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 a collaboration partner for sales and marketing. In addition, we intend to enter into collaborations 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 collaborations 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 collaboration 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 collaborations 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 collaboration 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;
- different payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;

- 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, natural disasters, including earthquakes, typhoons, floods and fires, public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic

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

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

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

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

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

RISKS RELATED TO OUR BUSINESS OPERATIONS AND INDUSTRY

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

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

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

As of June 30, 2021, we had 25 employees, all of which were full-time 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 civil, criminal and administrative 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, health information privacy and security laws and other privacy and security laws. If we are unable to comply, or have not fully complied, with such laws, we could face significant penalties, including criminal sanctions, civil penalties, contractual damages, reputational harm and diminished profits and future earnings.*

Our operations may be directly, or indirectly through our relationships with customers, third party payors, healthcare providers, and others 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 and other privacy requirements 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, including the civil False Claims Act, and civil monetary penalty laws, 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 ("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 Education and Clinical Health Act ("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 European General Data Protection Regulation ("GDPR") adopted by the European Union ("EU") in May 2018, which contains provisions specifically directed at the processing of health information and, more broadly, imposes significant and complex compliance burdens on processing personal data, with high sanctions and extra-territoriality measures intended to bring non-EU companies under the regulation's scope; we anticipate that over time we may expand our business operations to include additional operations in the EU, including potentially conducting preclinical and clinical trials and, with such expansion, we would be subject to increased governmental regulation in the EU countries in which we might operate, including but not limited to the GDPR;
- California enacted the California Consumer Privacy Act ("CCPA") in 2018, which created new individual privacy rights for consumers (as that word is broadly defined in the law) and placed increased privacy and security obligations on entities handling personal data of covered consumers or households. The CCPA, which went into effect on January 1, 2020, requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allows for a new cause of action for data breaches, which is expected to increase data breach class action litigation and may result in significant legal exposure. The CCPA's interpretation and enforcement remain uncertain, which further increases compliance costs. Although there are limited exemptions for clinical trial data under the CCPA, the CCPA and other similar laws may impact (possibly significantly) our business activities depending on how it is interpreted. Furthermore, it is anticipated that the California Privacy Rights Act of 2020 ("CCRA"), effective January 1, 2023, will expand the CCPA, and several other states have enacted or proposed data privacy laws, further exemplifying the evolving regulatory environment related to personal data and, particularly, protected 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 ("CMS") information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), and teaching hospitals, 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. Beginning in 2022, applicable manufacturers also will be required to report such information regarding its payment and other transfers of value to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives during the previous year; 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; state laws that require the reporting of information related to drug pricing; state and local laws that require the registration of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information and other sensitive 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, litigation, significant civil, criminal and administrative 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, including interrupting or stopping clinical trials, 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, in March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the "ACA") was passed and includes measures to significantly change the way healthcare is financed by both governmental and private insurers. There have been executive, judicial and Congressional challenges to certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, bills affecting the implementation of certain taxes under the ACA have been signed into law. Legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act ("Tax Act") includes a provision which repealed, 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". In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Further, prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began on February 15, 2021 and will remain open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the ACA and our business.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2030, except for a temporary suspension from May 1, 2020 through December 31, 2021 due to the COVID-19 pandemic, unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, further reduced Medicare payments to several

providers, including hospitals and cancer treatment centers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years.

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 federal and state legislative activity 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. For example, at the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, President Trump announced several executive orders related to prescription drug pricing that attempted to implement several of the Trump administration proposals. As a result, the FDA released a final rule, effective November 30, 2020, implementing a portion of the importation executive order providing guidance for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the U.S. Department of Health and Human Services (“HHS”) finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023. On November 20, 2020, CMS issued an interim final rule implementing President Trump’s Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries. The Most Favored Nation regulations mandate participation by identified Medicare Part B providers and will apply in all U.S. states and territories for a seven-year period beginning January 1, 2021 and ending December 31, 2027. On December 28, 2020, the United States District Court in the Northern District of California issued a nationwide preliminary injunction against implementation of the interim final rule. On January 13, 2021, in a separate lawsuit brought by industry groups in the U.S. District of Maryland, the government defendants entered a joint motion to stay litigation on the condition that the government would not appeal the preliminary injunction granted in the U.S. District Court for the Northern District of California and that performance for any final regulation stemming from the Most Favored Nation Model interim final rule shall not commence earlier than 60 days after publication of that regulation in the Federal Register. Based on a recent executive order, the Biden administration expressed its intent to pursue certain policy initiatives to reduce drug prices. 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.

In addition, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

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 security, confidentiality, integrity, and availability of our computer hardware, software, services, networks, communications, data, and Internet applications and related tools and functions, and those maintained on our behalf, could result in material adverse impact to our business, including without limitation a material interruption to our operations, including clinical trials, damage to our reputation and/or subject us to costs, fines or lawsuits.*

Our business requires manipulating, analyzing and storing large amounts of data, including personal data (including health information), intellectual property, trade secrets, and proprietary business information owned or controlled by ourselves or other parties. We also maintain personally identifiable information about our employees. We rely on a global enterprise software system to operate and manage our business, and our business therefore depends on the continuous, effective, reliable, and secure operation of our computer hardware, software, services, networks, communications, Internet servers and related infrastructure.

Cyberattacks, malicious internet-based activity and online and offline fraud are prevalent and continue to increase. In addition to traditional computer “hackers,” threat actors, software bugs, malicious code (such as viruses and worms), employee theft or misuse, denial-of-service attacks (such as credential stuffing), and ransomware attacks, sophisticated nation-state and nation-state supported actors now engage in attacks (including advanced persistent threat intrusions). We may also be the subject of phishing attacks, viruses, malware installation, server malfunction, software or hardware failures, loss of data or other computer assets, adware or other similar issues. Ransomware attacks are becoming increasingly prevalent and severe and can lead to significant interruptions, delays, or outages in our operations, disruption of clinical trials, loss of data (including data related to clinical trials), loss of income, significant extra expenses to restore data or systems, reputational loss and the diversion of funds. To alleviate the impact of a ransomware attack it may be preferable to make extortion payments, but we may be unwilling or unable to do so (including, for example, if applicable laws or regulations prohibit such payments). Similarly, supply chain attacks have increased in frequency. Despite security controls we have in place, such attacks are difficult to avoid.

Any of the aforementioned threats could cause a security incident, which, in turn, could result in unauthorized access to, damage to, disablement or encryption of, use or misuse of, disclosure of, modification of, destruction of, or loss of our data or our customers’ data, or disrupt our ability to provide our services or our service providers’ ability to support our services. As a result, our business could suffer. The integrity and protection of our sensitive data, including employee and personal health information, is critical to our business, and employees and others have a high expectation that we will adequately protect their personal information.

We may expend significant resources, fundamentally change our business activities and practices, or modify our operations, including our clinical trial activities, or information technology in an effort to protect against security incidents and to mitigate, detect, and remediate actual and potential vulnerabilities. Applicable data protection laws, privacy policies or other obligations related to data privacy (e.g. contractual obligations, obligations related to membership in industry organizations) may require us to implement specific security measures or use industry-standard or reasonable measures to protect against security measures. 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.

While we have implemented security measures designed to protect against a security incident, there can be no assurance that our security measures or those of our partners will be effective in protecting against a security incident. We may be unable

in the future to detect, anticipate, measure or prevent threats or techniques used to detect or exploit vulnerabilities in our (or our partners') information technology, services, communications or software because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after an incident has occurred.

If we, or a third party upon whom we rely, experience a security incident, or are perceived to have experienced a security incident, it may result in: government enforcement actions that could include investigations, fines, penalties, audits and inspections; additional reporting requirements and/or oversight; temporary or permanent bans on all or some processing of personal data (which could impact our clinical trials or training of our algorithm); or orders to destroy or not use personal data. Further, individuals or other relevant stakeholders could sue us for our actual or perceived failure to comply with our security obligations, including, without limitation, in class action litigation. We may also need to notify relevant stakeholders in the event of a security incident, as required by applicable laws, which is costly and could damage our reputation. Security incidents could also result in indemnity obligations, negative publicity and financial loss.

Furthermore, there can be no assurance that the limitations of liability in our contracts would be enforceable or adequate or otherwise protect us from liabilities or damages if we fail to comply with applicable data protection laws, privacy policies or data protection obligations related to information security or security incident. Additionally, we cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or adequately mitigate liabilities or damages with respect to claims, costs, expenses, litigation, fines, penalties, business loss, data loss, regulatory actions or material adverse impacts arising out of our privacy and security practices, processing or security incidents we may experience, or that such coverage will continue to be available on commercially reasonable terms or at all.

Changes in funding for FDA, the SEC and other government agencies could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept payment of user fees, and statutory, regulatory, and policy changes. Average review times at the agency have fluctuated in recent years as a result. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities is subject to the political process, which is inherently fluid and unpredictable.

Disruptions at the FDA and other agencies may also slow the time necessary for new drugs to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. For example, over the last several years, the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

The withdrawal of the United Kingdom from the European Union, commonly referred to as "Brexit," may adversely impact our ability to obtain regulatory approvals of our product candidates in the European Union, result in restrictions or imposition of taxes and duties for importing our product candidates into the European Union, and may require us to incur additional expenses in order to develop, manufacture and commercialize our product candidates in the European Union.

Following the result of a referendum in 2016, the United Kingdom left the European Union on January 31, 2020, commonly referred to as "Brexit." Pursuant to the formal withdrawal arrangements agreed between the United Kingdom and the European Union, the United Kingdom was subject to a transition period that ended December 31, 2020, or the Transition Period, during which EU rules continued to apply. A trade and cooperation agreement, or the Trade and Cooperation Agreement, that outlines the future trading relationship between the United Kingdom and the European Union was agreed in December 2020.

Since a significant proportion of the regulatory framework in the United Kingdom applicable to our business and our product candidates is derived from EU directives and regulations, Brexit has had, and may continue to have, a material impact upon the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our product candidates in the United Kingdom or the European Union. For example, Great Britain is no longer covered by the centralized procedures for obtaining EU-wide marketing authorization from the EMA and a separate marketing authorization

will be required to market our product candidates in Great Britain. It is currently unclear whether the Medicines & Healthcare products Regulatory Agency ("MHRA"), in the U.K. is sufficiently prepared to handle the increased volume of marketing authorization applications that it is likely to receive. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, would prevent us from commercializing our product candidates in the United Kingdom or the European Union and restrict our ability to generate revenue and achieve and sustain profitability.

While the Trade and Cooperation Agreement provides for the tariff-free trade of medicinal products between the UK and the EU there may be additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period. Further, should the UK diverge from the EU from a regulatory perspective in relation to medicinal products, tariffs could be put into place in the future. We could therefore, both now and in the future, face significant additional expenses (when compared to the position prior to the end of the Transition Period) to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the UK. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the EU. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the United Kingdom.

Our business and operations might be disrupted or adversely affected by catastrophic events.

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. In addition, natural disasters or other catastrophic events in various parts of the world, including interruptions in the supply of natural resources, political and governmental changes, disruption in transportation networks or delivery services, severe weather conditions, wildfires and other fires, explosions, actions of animal rights activists, terrorist attacks, earthquakes, wars and public health issues (including, for example, the COVID-19 pandemic) could disrupt our operations or those of our collaborators, contractors and vendors or contribute to unfavorable economic or other conditions that could adversely impact us.

Our business could be adversely affected by the effects of health pandemics or epidemics, including the ongoing COVID-19 pandemic, in regions where we or third parties on which we rely have significant manufacturing facilities, concentrations of clinical trial sites or other business operations, or materially affect our operations globally, including at our headquarters in San Diego and at our clinical trial sites, as well as the business or operations of our collaborators, manufacturers, CROs or other third parties with whom we conduct business.*

Our business may be adversely affected by the effects of health pandemics or epidemics, including the COVID-19 pandemic. The ongoing COVID-19 pandemic is impacting domestic and worldwide economic activity, including global financial markets. The COVID-19 pandemic also poses the risk that we or our clinical trial subjects, employees, contractors, collaborators and vendors may be prevented from conducting certain clinical trials or other business activities for an indefinite period of time, including due to travel restrictions, quarantines, "stay-at-home" and "shelter-in-place" orders or shutdowns that have been or may in the future be requested or mandated by governmental authorities. In addition, the COVID-19 pandemic has, and could continue to, impact personnel at third-party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which could potentially disrupt the supply chain for our product candidates in our collaborators' ongoing clinical trials. For example, some of our CROs have previously delayed the commencement of preclinical studies due to shelter-in-place orders. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition.

In addition, our clinical trials have been, and are likely to continue to be, affected by the ongoing COVID-19 pandemic. Site initiation and patient enrollment may be delayed due to prioritization of hospital resources toward the COVID-19 pandemic, and some patients may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Similarly, our ability to recruit and retain patients and principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, could be delayed or disrupted, which would adversely impact our clinical trial operations.

While the long-term economic impact and the duration of the COVID-19 pandemic may be difficult to predict, the pandemic has resulted in, and may continue to result in, significant disruption of global financial markets, which could reduce our ability to access capital and could negatively affect our liquidity and the liquidity and stability of markets for our common

stock and convertible notes. The spread of COVID-19, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic, may be difficult to assess or predict, there have previously been significant disruptions of global financial markets as a result of the COVID-19 pandemic and similar disruptions may be experienced in the future. Any such disruption could make it more difficult for us to access capital or to comply with the covenants contained in the Loan Agreement, which could negatively affect our liquidity. In addition, a recession or market correction resulting from the spread of COVID-19 could materially affect our business and the value of our common stock.

The COVID-19 pandemic continues to evolve. The ultimate impact of the COVID-19 pandemic or a similar health pandemic or epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. These effects could have a material impact on our operations, and we will continue to monitor the COVID-19 situation closely.

RISKS RELATED TO OUR COMMON STOCK

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

Our stock price has historically been, and is expected to continue to be, highly volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in preclinical studies or clinical trials;
- inability to obtain additional funding;
- any delay in filing an IND or NDA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND or NDA;
- failure to maintain our existing collaborations or enter into new collaborations;
- failure of our collaboration partners to elect to develop and commercialize product candidates under our collaboration agreements or the termination of any programs under our collaboration agreements;
- failure by us or our licensors and collaboration 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;
- changes in the structure of healthcare payment systems;
- 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;
- disruptions caused by man-made or natural disasters, public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us, our collaboration 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 Capital Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

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

Our common stock is currently listed on The Nasdaq Capital Market. In order to maintain the listing of our common stock on The Nasdaq Capital Market, 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 and a minimum stockholders' equity requirement of \$2.5 million.

We have failed to comply with Nasdaq's minimum bid price requirement and minimum stockholders' equity requirement on multiple other occasions during the last several years. Most recently, on August 9, 2021, 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 price required for continued listing on The Nasdaq Capital Market, and therefore we could become subject to delisting if our common stock does not meet the \$1.00 minimum bid price for a minimum of 10 consecutive trading days within the 180-day period following the date of the letter, or within an additional 180-day period if we meet certain conditions. We intend to monitor the closing bid price of our common stock and may, if appropriate, consider implementing available options, including a reverse stock split, to regain compliance with the minimum closing bid price requirement. There can be no assurance that we will be able to regain and maintain compliance with the \$1.00 minimum bid price requirement or maintain compliance with the minimum stockholders' equity requirement, or continuously satisfy Nasdaq's other continued listing standards in the future. If we are ultimately not able to maintain or timely regain compliance with Nasdaq's continued listing requirements, our common stock will 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 Capital Market would constitute an event of default under our Loan Agreement with the Lender.

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 Capital Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (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 ("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.

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.*

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. As of June 30, 2021, warrants to exercise an aggregate of 61.9 million shares of our common stock were outstanding at a weighted-average exercise price per share of \$0.78. In addition, as of June 30, 2021, an aggregate of 18.5 million shares were issuable upon conversion of shares of our Class A-1, Class A-2 and Class A-3 preferred stock at the option of the holder, subject to beneficial ownership limitations.

Pursuant to our 2019 Equity Incentive Plan (the "2019 Plan"), our management is authorized to grant stock options and other equity-based awards to our employees, directors and consultants. In addition, the number of shares available for future grant under the 2019 Plan will automatically increase on January 1st each year commencing on January 1, 2021 through January 1, 2029, by 5% 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. Furthermore, 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 ("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 lesser of 1% of the total number of shares of our common stock outstanding on December 31st of the preceding calendar year and 41,666 shares, subject to the ability of our board of directors to take action to reduce the size of the increase in any given year. Currently, we plan to register the increased number of shares available for issuance under the 2019 Plan and the ESPP each year.

We may be the subject of putative securities class action litigation 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. For example, certain putative class action complaints were filed against us, Paul C. Grint (our former Chief Executive Officer), Joseph P. Hagan (then our Chief Operating Officer and currently our President and Chief Executive Officer), Timothy M. Wright (or former Chief Research & Development Officer) and Michael Huang (our former Vice President of Clinical Development) in January 2017 alleging that 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. On December 29, 2020, the court entered a final judgment and dismissed the action with prejudice. 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.

Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flow, financial condition or results of operations.*

New income, sales, use or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business operations and financial performance. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, the Tax Act enacted many significant changes to the U.S. tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to the Tax Act may affect us, and certain aspects of the Tax Act could be repealed or modified in future legislation. For example, the CARES Act modified certain provisions of the Tax Act. In addition, it is uncertain if and to what extent various

states will conform to the Tax Act, the CARES Act, or any newly enacted federal tax legislation. Changes in corporate tax rates, the realization of net deferred tax assets relating to our operations, the taxation of foreign earnings, and the deductibility of expenses under the Tax Act or future reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future U.S. tax expense.

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

As of December 31, 2020, we had net operating loss ("NOL") carryforwards for U.S. federal and California state tax purposes of \$342.4 million and \$289.2 million, respectively. A portion of the federal and California state NOL carryforwards will begin to expire, if not utilized, in 2030 and 2031, respectively. NOLs that expire unused will be unavailable to offset future income tax liabilities. Under the Tax Act, as modified by the CARES ACT, federal NOLs incurred in taxable years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOLs in tax years beginning after December 31, 2020 is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to the Tax Act or the CARES Act. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended (the "Code"), 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 NOL carryforwards and other pre-change tax attributes (such as research tax credits) to offset its post-change income and taxes may be limited. We have determined that we triggered an "ownership change" limitation at the completion of our initial public offering in October 2012 and in July 2015. The Company has not performed a Section 382 ownership-change analysis through December 31, 2020, and it is possible there may have been additional ownership changes. 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 NOL carryforwards to offset U.S. federal taxable income will be subject to limitations, which could harm our future operating results by effectively increasing our future tax obligations. 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. For example, California imposed limits on the usability of California state net operating losses to offset taxable income in tax years beginning after 2019 and before 2023. As a result, if we earn net taxable income, we may be unable to use all or a material portion of our net operating loss carryforwards and other tax attributes, which could potentially result in increased future tax liability to us and adversely affect our future cash flows.

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

During the three months ended June 30, 2021, we issued (i) 75,850 shares of our common stock upon conversion of 7,585 shares of our Class A-2 preferred stock, pursuant to the election of the holder and (ii) 250,000 shares of our common stock upon the exercise of common stock warrants originally issued in December 2020 pursuant to our private placement transaction. In each case, the shares of common stock were issued in reliance on Section 3(a)(9) of the Securities Act of 1933, as amended.

ITEM 3. DEFAULTS UPON SENIOR SECURITIES

None.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

On August 9, 2021, we received a letter (the "Notice") from The Nasdaq Stock Market ("Nasdaq") advising us that for 30 consecutive trading days preceding the date of the Notice, the bid price of our common stock had closed below the \$1.00 per share minimum required for continued listing on The Nasdaq Capital Market pursuant to Nasdaq Listing Rule 5550(a)(2) (the "Minimum Bid Price Requirement").

The Notice has no effect on the listing of our common stock at this time, and our common stock continues to trade on The Nasdaq Capital Market under the symbol "RGLS."

Under Nasdaq Listing Rule 5810(c)(3)(A), if during the 180 calendar day period following the date of the Notice (the "Compliance Period") the closing bid price of our common stock is at or above \$1.00 for a minimum of 10 consecutive business days, we will regain compliance with the Minimum Bid Price Requirement and our common stock will continue to be eligible for listing on The Nasdaq Capital Market absent noncompliance with any other requirement for continued listing.

If we do not regain compliance with the Minimum Bid Price Requirement by the end of the Compliance Period, under Nasdaq Listing Rule 5810(c)(3)(A) (ii) if on the last day of the Compliance Period we are in compliance with the market value of publicly held shares requirement for continued listing as well as all other standards for initial listing of our common stock on The Nasdaq Capital Market (other than the Minimum Bid Price Requirement), we will be afforded an additional 180 day compliance period (the "Additional Compliance Period"), unless we do not indicate our intent to cure the deficiency, or if it does not appear to Nasdaq that it is possible for us to cure the deficiency, in which case we will not be eligible for the Additional Compliance Period.

If we do not regain compliance with the Minimum Bid Price Requirement by the end of the Compliance Period, or the Additional Compliance Period, if applicable, our common stock will be subject to delisting.

We intend to monitor the closing bid price of our common stock and may, if appropriate, consider implementing available options, including a reverse stock split, to regain compliance with the Minimum Bid Price Requirement.

ITEM 6. EXHIBITS

Exhibit Number	Description
3.1	<u>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).</u>
3.2	<u>Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on October 2, 2018).</u>
3.3	<u>Certificate of Amendment of Amended and Restated Certificate of Incorporation of the Registrant. (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on June 16, 2021).</u>
3.4	<u>Certificate of Designation of Preferences, Rights and Limitations of Class A-1 Convertible Preferred Stock (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 May 9, 2019).</u>
3.5	<u>Certificate of Designation of Preferences, Rights and Limitations of Class A-2 Convertible Preferred Stock (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 December 26, 2019).</u>
3.6	<u>Certificate of Designation of Preferences, Rights and Limitations of Class A-3 Convertible Preferred Stock (incorporated by reference to Exhibit 3.1 to the Registrants' Current Report on Form 8-K (File No. 001-35670) filed with the SEC on December 4, 2020).</u>
3.7	<u>Certificate of Amendment to the Certificate of Designation of Preferences, Rights and Limitations of Class A-1 Convertible Preferred Stock (incorporated by reference to Exhibit 3.2 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on December 4, 2020).</u>
3.8	<u>Certificate of Amendment to the Certificate of Designation of Preferences, Rights and Limitations of Class A-2 Convertible Preferred Stock (incorporated by reference to Exhibit 3.3 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on December 4, 2020).</u>
3.9	<u>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).</u>
4.1	Reference is made to Exhibits <u>3.1</u> , <u>3.2</u> , <u>3.3</u> , <u>3.4</u> , <u>3.5</u> , <u>3.6</u> , <u>3.7</u> , <u>3.8</u> and <u>3.9</u> .
4.2	<u>Form of Common Stock Certificate of the Registrant (incorporated by reference to Exhibit 4.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-35670), filed with the SEC on November 9, 2018).</u>
4.3	<u>Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on May 9, 2019).</u>
4.4	<u>Form of Common Stock Purchase Warrant (incorporated by reference to Exhibit 4.2 to the Registrant's Current Report on Form 8-K (File No. 001-35670), filed with the SEC on December 4, 2020).</u>
5.1	<u>Opinion of Cooley LLP.</u>

31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Securities Exchange Act of 1934.
32.1**	Certification of the Chief Executive Officer and Chief 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.
104	The cover page from the Registrant's Quarterly Report on Form 10-Q has been formatted in Inline XBRL.

** 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.

Date: August 10, 2021	Regulus Therapeutics Inc. By: <u>/s/ Joseph P. Hagan</u> Joseph P. Hagan President and Chief Executive Officer (Principal Executive Officer)
Date: August 10, 2021	By: <u>/s/ Cris Calsada</u> Cris Calsada Chief Financial Officer (Principal Financial Officer)



Thomas A. Coll
+1 858 550 6013
collta@cooley.com

August 10, 2021
Regulus Therapeutics Inc.
4224 Campus Point Court, Suite 210
San Diego, CA 92121

Ladies and Gentlemen:

We have acted as counsel to Regulus Therapeutics Inc., a Delaware corporation (the "**Company**"), with respect to certain matters in connection with the offering by the Company of \$50,000,000 (full amount) of shares of the Company's common stock, par value \$0.001 per share (the "**Shares**"), pursuant to the Registration Statement on Form S-3 (File No. 333-254063) (the "**Registration Statement**"), filed with the Securities and Exchange Commission (the "**Commission**") under the Securities Act of 1933, as amended (the "**Act**"), the related prospectus dated March 9, 2021 included within the Registration Statement (the "**Base Prospectus**"), and the prospectus supplement dated August 10, 2021, filed with the Commission pursuant to Rule 424(b) of the Rules and Regulations of the Act (together with the Base Prospectus, the "**Prospectus**"). The Shares are to be sold by the Company in accordance with that certain Sales Agreement, dated December 12, 2018, by and between the Company and H.C. Wainwright & Co., LLC (the "**Agreement**"), as described in the Prospectus.

In connection with this opinion, we have examined and relied upon the Registration Statement, the Prospectus, the Agreement, the Company's Amended and Restated Certificate of Incorporation, as amended, and its Amended and Restated Bylaws, each as currently in effect, and such other documents, records, certificates, memoranda and other instruments as in our judgment are necessary or appropriate to render the opinion expressed below. In rendering this opinion, we have assumed the genuineness and authenticity of all signatures on original documents; the genuineness and authenticity of all documents submitted to us as originals; the conformity to originals of all documents submitted to us as copies; and the accuracy, completeness and authenticity of certificates of public officials. As to certain factual matters, we have relied upon a certificate of an officer of the Company and have not sought independently to verify such matters.

We have assumed that each sale of the Shares will be duly authorized by the Board of Directors of the Company, a duly authorized committee thereof or a person or body pursuant to an authorization granted in accordance with Section 152 of the General Corporation Law of the State of Delaware (the "**DGCL**") and that no more than 120,000,000 Shares will be sold under the Agreement. We express no opinion to the extent that future issuances of securities of the Company and/or anti-dilution adjustments to outstanding securities of the Company cause the number of shares of the Company's common stock outstanding or issuable upon conversion or exercise of outstanding securities of the Company to exceed the number of Shares then issuable under the Agreement.

Our opinion herein is expressed solely with respect to the DGCL. Our opinion is based on these laws as in effect on the date hereof, and we disclaim any obligation to advise you of facts, circumstances, events or developments which hereafter may be brought to our attention and which may alter, affect or modify the opinion expressed herein. We express no opinion as to whether the laws of any particular jurisdiction other than those identified above are applicable to the subject matter hereof. We are not rendering any

Cooley LLP 4401 Eastgate Mall San Diego, CA 92121
t: (858) 550-6000 f: (858) 550-6420 cooley.com

[Redacted signature box]



Regulus Therapeutics

August 10, 2021

Page Two

opinion as to compliance with any federal or state law, rule or regulation relating to securities, or to the sale or issuance thereof.

On the basis of the foregoing, and in reliance thereon, and subject to the qualifications herein stated, we are of the opinion that the Shares, when sold and issued against payment therefor in accordance with the Agreement, the Registration Statement and the Prospectus, will be validly issued, fully paid and nonassessable.

We consent to the reference to our firm under the caption "Legal Matters" in the Prospectus and to the filing of this opinion as an exhibit to a Current Report on Form 8-K to be filed with the Commission for incorporation by reference into the Registration Statement.

Sincerely,

Cooley LLP

By: /s/ Thomas A. Coll
Thomas A. Coll

Cooley LLP 4401 Eastgate Mall San Diego, CA 92121
t: (858) 550-6000 f: (858) 550-6420 cooley.com

[Redacted signature area]

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

I, Joseph P. Hagan, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Regulus Therapeutics Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13(a)-15(f) and 15(d)-15(f)) for the registrant and have:
 - a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

August 10, 2021

/s/ Joseph P. Hagan

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

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

I, Cris Calsada, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Regulus Therapeutics Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13(a)-15(f) and 15(d)-15(f)) for the registrant and have:
 - a. designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b. designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c. evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d. disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a. all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b. any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

August 10, 2021

/s/ Cris Calsada

Cris Calsada
Chief Financial Officer
(Principal Financial Officer)

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

In connection with the quarterly report of Regulus Therapeutics Inc. (the "Company") on Form 10-Q for the quarter ended June 30, 2021 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Joseph P. Hagan, President and Chief Executive Officer of the Company, and I, Cris Calsada, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

- (1) The Report fully complies with the requirements of Section 13(a) or 15(d), as applicable, of the Securities Exchange Act of 1934, as amended; and
- (2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

August 10, 2021

/s/ Joseph P. Hagan

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

August 10, 2021

/s/ Cris Calsada

Cris Calsada
Chief Financial Officer
(Principal Financial Officer)

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